



















# HEART.

## A JOURNAL FOR THE STUDY OF THE CIRCULATION.

EDITED BY

THOMAS LEWIS, M.D.,

AIDED IN THE SELECTION OF PAPERS BY

Dr. W. H. GASKELL.

Prof. A. R. CUSHNY (London).  
Dr. LEONARD HILL (London).  
Dr. J. MACKENZIE (London).

Prof. A. W. HEWLETT (Ann Arbor)  
Prof. G. N. STEWART (Cleveland).

WITH THE COLLABORATION OF

Prof. J. G. ADAMI (Montreal).  
Sir T. CLIFFORD ALLBUTT (Cambridge).  
Prof. L. ASCHOFF (Freiburg).  
Prof. W. M. BAYLISS (London).  
Dr. C. BOLTON (London).  
Sir JOHN ROSE BRADFORD (London).  
Dr. W. LANGDON BROWN (London).  
Sir LAUDER BRUNTON, Bt. (London).  
Dr. W. J. CALVERT (Dallas).  
Prof. A. J. CARLSON (Chicago).  
Dr. ALEXIS CARREL (New York).  
Dr. A. E. COHN (New York).  
Dr. C. M. COOPER (San Francisco).  
Dr. JOHN COWAN (Glasgow).  
Prof. GEORGE W. CRILE (Cleveland).  
Prof. HARVEY CUSHING (Baltimore).  
Dr. GEORGE DOCK (St. Louis).  
Prof. W. EINTHOVEN (Leyden).  
Prof. J. ERLANGER (St. Louis).  
Dr. A. G. GIBSON (Oxford).  
Dr. G. A. GIBSON (Edinburgh).  
Dr. A. M. GOSSAGE (London).  
Prof. F. GOTCH (Oxford).

Prof. T. WARDROP GRIFFITH (Leeds).  
Prof. CH. C. GUTHRIE (Pittsburg).  
Dr. J. HAY (Liverpool).  
Prof. Y. HENDERSON (New Haven).  
Dr. W. P. HERRINGHAM (London).  
Dr. A. D. HIRSCHFELDER (Baltimore).  
Prof. CH. F. HOOVER (Cleveland).  
Prof. WM. H. HOWELL (Baltimore).  
Prof. T. C. JANEWAY (New York).  
Prof. A. KEITH (London).  
Prof. J. A. MACWILLIAM (Aberdeen).  
Dr. S. J. MELTZER (New York).  
Prof. JOSEPH L. MILLER (Chicago).  
Sir R. DOUGLAS POWELL, Bt. (London).  
Dr. W. T. RITCHIE (Edinburgh).  
Prof. TORALD SOLLMANN (Cleveland).  
Prof. E. H. STARLING (London).  
Prof. GRAHAM STEELL (Manchester).  
Prof. W. S. THAYER (Baltimore).  
Prof. A. D. WALLER (London).  
Prof. G. S. WOODHEAD (Cambridge).  
Sir ALMROTH E. WRIGHT (London).

VOL. IV.

1912-1913.

London:

SHAW & SONS, FETTER LANE, FLEET STREET, E.C.

1913

139796  
3/10/16



RC

681

AIH38

v.4



# CONTENTS OF VOL. IV.

No. 1 (Issued November 2, 1912).

|   | PAGE |
|---|------|
| THE RELATION OF THE AURICULO-VENTRICULAR REGION TO THE SEQUENCE OF CONTRACTION OF THE HEART. By George S. Bond. ( <i>Johns Hopkins University</i> ) .. .. .   | 1    |
| A DESCRIPTION OF A CASE OF COMPLETE HEART-BLOCK, INCLUDING THE POST-MORTEM EXAMINATION. By Alfred E. Cohn ( <i>from the Hospital of the Rockefeller Institute for Medical Research</i> ) and Thomas Lewis ( <i>from the Cardiographic Department, University College Hospital Medical School</i> ) .. .. .  | 7    |
| AURICULAR FIBRILLATION AND COMPLETE HEART-BLOCK. A DESCRIPTION OF A CASE OF ADAMS-STOKES' SYNDROME, INCLUDING THE POST-MORTEM EXAMINATION. By Alfred E. Cohn ( <i>from the Hospital of the Rockefeller Institute for Medical Research</i> ) and Thomas Lewis ( <i>from the Cardiographic Department, University College Hospital Medical School</i> ) .. .. . | 15   |
| THE ACTION OF DIGITALIS IN THERAPEUTICS. By A. R. Cushny, H. F. Marris and M. D. Silberberg. ( <i>From the Heart Wards of Mount Vernon Hospital and the Pharmacological Department of University College, London</i> ).. .. .   | 33   |
| CARDIAC IRREGULARITIES IN MORPHINE POISONING IN THE DOG. By J. A. E. Eyster and W. J. Meek. ( <i>From the Physiological Laboratory of the University of Wisconsin</i> ) .. .. .   | 59   |
| TWO MODES OF CLOSURE OF THE HEART VALVES. By Yandell Henderson and F. Elmer Johnson. ( <i>From the Physiological Laboratory of the Yale Medical School</i> ) .. .. .  | 69   |
| ON THE SYSTOLIC BLOOD-PRESSURE IN THE ARM AND LEG IN AORTIC INCOMPETENCE. By H. D. Rolleston. ( <i>St. George's Hospital, London</i> ) .. .. .  | 83   |
| OBSERVATIONS ON A CASE OF AURICULAR FIBRILLATION WITH SLOW VENTRICULAR ACTION. By A. W. Falconer and George Dean. ( <i>Aberdeen</i> ) .. .. .   | 87   |
| RHYTHMIC CHANGES IN THE HUMAN HEART BEAT. By G. Canby Robinson and George Draper. ( <i>From the Hospital of the Rockefeller Institute for Medical Research, New York</i> ) .. .. .  | 97   |

No. 2 (Issued November 30, 1912).

|   |     |
|---|-----|
| EXTRASYSTOLE AND THE STAIRCASE PHENOMENON. By E. W. Goteling Vinnis. ( <i>The Hague</i> ) .. .. .   | 123 |
| PAROXYSMAL TACHYCARDIA. By T. Stuart Hart. ( <i>New York</i> ) ( <i>From the Second Medical Division of the Presbyterian Hospital</i> ) .. .. .   | 128 |
| OBSERVATIONS ON A CASE PRESENTING A LONG A-C INTERVAL, ASSOCIATED WITH SHORT PAROXYSMS OF TACHYCARDIA ARISING IN THE JUNCTIONAL TISSUES. By A. W. Falconer and George Dean. ( <i>Aberdeen</i> ) .. .. . | 137 |



# CONTENTS.

PAGE

|   |     |
|---|-----|
| ON SIMULTANEOUS RECORDS OF THE HEART SOUNDS AND THE ELECTROCARDIOGRAM. By George Fahr. ( <i>From the Physiological Laboratory of the University of Leyden</i> ) . . . . .   | 147 |
| OBSERVATIONS UPON A CURIOUS AND NOT UNCOMMON FORM OF EXTREME ACCELERATION OF THE AURICLE. "AURICULAR FLUTTER." By Thomas Lewis. ( <i>Cardiographic Department, University College Hospital Medical School</i> ) . . . . .                     | 171 |
| No. 3 (Issued May 29, 1913).  |     |
| THE POST-MORTEM EXAMINATION OF HORSES' HEARTS FROM CASES OF AURICULAR FIBRILLATION. By Alfred E. Cohn. ( <i>From the Hospital of the Rockefeller Institute for Medical Research</i> ) . . . . .   | 221 |
| OBSERVATIONS ON INJECTION SPECIMENS OF THE CONDUCTION SYSTEM IN OX HEARTS. By Alfred E. Cohn. ( <i>From the Hospital of the Rockefeller Institute for Medical Research</i> ) . . . . .  | 225 |
| FURTHER OBSERVATIONS UPON THE ISOLATED APEX PREPARATION IN THE FROG'S HEART. By G. H. Clark and Williamina Abel. ( <i>From the Physiology Department of the University of Glasgow</i> ) . . . . .   | 231 |
| THE TIME RELATIONS OF HEART SOUNDS AND MURMURS, WITH SPECIAL REFERENCE TO THE ACOUSTIC SIGNS IN MITRAL STENOSIS. By Thomas Lewis. ( <i>From the Cardiographic Department, University College Hospital Medical School</i> ) . . . . .          | 241 |
| SOME PROPERTIES OF SURVIVING ARTERIES. By J. Elrick Kesson, M.D., <i>Lecturer on Experimental Physiology in the University of Aberdeen.</i> ( <i>From the Physiological Laboratory</i> ) . . . . .  | 259 |
| AN OBSERVATION RELATING TO THE NATURE OF AURICULAR FIBRILLATION. By Thomas Lewis. ( <i>Cardiographic Department, University College Hospital Medical School</i> ) . . . . .   | 273 |
| THE ESTIMATION OF SYSTOLIC BLOOD-PRESSURE IN MAN WITH SPECIAL REFERENCE TO THE INFLUENCE OF THE ARTERIAL WALL. By J. A. MacWilliam and J. E. Kesson. ( <i>From the Physiological Laboratory of the University of Aberdeen</i> ) . . . . .     | 279 |
| No. 4 (Issued June 14, 1913).   |     |
| THE EXCITING CAUSES OF VENTRICULAR FIBRILLATION IN ANIMALS UNDER CHLOROFORM ANÆSTHESIA. By A. Goodman Levy. ( <i>From the Research Laboratories of the Medical School, University College Hospital</i> ) . . . . .                            | 319 |
| THE INFLUENCE OF INCREASE OF TEMPERATURE UPON THE INHIBITORY MECHANISM OF THE HEART OF THE MAMMAL. By G. H. Clark. ( <i>From the Department of Physiology, University of Glasgow</i> ) . . . . .  | 379 |
| LESIONS OF THE BRANCHES OF THE AURICULO-VENTRICULAR BUNDLE. By George D. Mathewson. ( <i>From the Clinical Research Laboratory of the Royal Infirmary, Edinburgh</i> ) . . . . .  | 385 |
| THE CONDUCTION OF THE PULSE WAVE AND ITS RELATION TO THE ESTIMATION OF SYSTOLIC BLOOD-PRESSURE. By J. A. MacWilliam, J. E. Kesson and G. Spencer Melvin. ( <i>From the Physiological Laboratory of the University of Aberdeen</i> ) . . . . . | 393 |



# LIST OF AUTHORS.

---

|   | PAGE |
|---|------|
| BOND, GEORGE S. "The Relation of the Auriculo-Ventricular Region to the Sequence of Contraction of the Heart" .. .. .                             | 1    |
| CLARK G. H. "The Influence of Increase of Temperature upon the Inhibitory Mechanism of the Heart of the Mammal" .. .. .                           | 379  |
| CLARK, G. H., AND ABEL, WILLIAMINA. "Further Observations upon the Isolated Apex Preparation in the Frog's Heart" .. .. .                         | 231  |
| COHN, ALFRED E. "Observations on Injection Specimens of the Conduction System in Ox Hearts" .. .. .   | 225  |
| "The Post-Mortem Examination of Horses' Hearts from Cases of Auricular Fibrillation" .. .. .  | 221  |
| COHN, ALFRED E., AND LEWIS, THOMAS. "A Description of a Case of Complete Heart-Block, including the Post-Mortem Examination" .. .. .              | 7    |
| "Auricular Fibrillation and Complete Heart-Block. A Description of a Case of Adams-Stokes' Syndrome, including the Post-Mortem Examination" ..    | 15   |
| CUSHNY, A. R., MARRIS, H. F., AND SILBERBERG, M. D. "The Action of Digitalis in Therapeutics" .. .. .   | 33   |
| EYSTER, J. A. E., AND MEEK, W. J. "Cardiac Irregularities in Morphine Poisoning in the Dog" .. .. .   | 59   |
| FAHR, GEORGE. "On Simultaneous Records of the Heart Sounds and the Electro-cardiogram" .. .. .  | 147  |
| "Observations on a Case presenting a long A-C Interval, associated with Short Paroxysms of Tachycardia arising in the Junctional Tissues" .. .. . | 137  |
| FALCONER, A. W., AND DEAN, GEORGE. "Observations on a Case of Auricular Fibrillation with Slow Ventricular Action" .. .. .                        | 87   |
| HART, T. STUART. "Paroxysmal Tachycardia" .. .. .   | 128  |
| HENDERSON, YANDELL, AND JOHNSON, F. ELMER. "Two Modes of Closure of the Heart Valves" .. .. .   | 69   |
| KESSON, J. ELRICK, M.D. "Some Properties of Surviving Arteries" .. .. .   | 259  |

# LIST OF AUTHORS.

|  | PAGE |
|--|------|
| LEVY, A. GOODMAN. "The Exciting Causes of Ventricular Fibrillation in Animals under Chloroform Anæsthesia" .. .. .   | 319  |
| LEWIS, THOMAS. "An Observation Relating to the Nature of Auricular Fibrillation"   | 273  |
| "Observations upon a Curious and not Uncommon Form of Extreme Acceleration of the Auricle. 'Auricular Flutter'" .. .. .                                      | 171  |
| "The Time Relations of Heart Sounds and Murmurs, with Special Reference to the Acoustic Signs in Mitral Stenosis" .. .. .                                    | 241  |
| MACWILLIAM, J. A., AND KESSON, J. E. "The Estimation of Systolic Blood-Pressure in Man with Special Reference to the Influence of the Arterial Wall" .. .. . | 279  |
| MACWILLIAM, J. A., KESSON, J. E., AND MELVIN, G. SPENCER. "The Conduction of the Pulse Wave and its Relation to the Estimation of Systolic Blood-Pressure"   | 393  |
| MATHEWSON, GEORGE D. "Lesions of the Branches of the Auriculo-Ventricular Bundle" .. .. .  | 385  |
| ROBINSON, G. CANBY, AND DRAPER, GEORGE. "Rhythmic Changes in the Human Heart Beat" .. .. .   | 97   |
| ROLLESTON, H. D. "On the Systolic Blood-Pressure in the Arm and Leg in Aortic Incompetence" .. .. .  | 83   |
| VINNIS, E. W. GOTELING. "Extrasystole and the Staircase Phenomenon" .. .. .  | 123  |



# THE RELATION OF THE AURICULO-VENTRICULAR REGION TO THE SEQUENCE OF CONTRACTION OF THE HEART.

By GEORGE S. BOND.

(*Johns Hopkins University.*)

THE auriculo-ventricular region has long been a subject for dispute, particularly as to the relation it bears to the sequence of contraction of the heart. Physiologists are still debating whether the transmission of the stimulus at this point is through neural or muscular paths. The evidence, however, points to the latter as the true mode of conduction, but if this be true another question arises. What is the cause for the long pause that occurs at that point? Delay in transmission, due simply to the change in number and direction of muscular fibres, is hardly a sufficient explanation.

Clinicians too are especially interested in this portion of the heart. Its association with heart-block and the possibilities it holds of explaining some of the numerous irregularities, give it special emphasis. For this reason any facts, however small, are worthy of note, which throw light upon the action of this region during the contraction of the heart. Therefore I wish to record certain observations which I have made upon the frog's heart, in the hope that they may aid in the further study of this region in the mammalian heart.

During the year 1910, I undertook some investigations on the septal nerves of the frog's heart. I followed the experiments used by F. B. Hofmann and my results coincided with those he obtained. These show that the septal nerves carry the fibres of the vagus which control the strength of contraction and tonicity rather than those affecting rhythmicity.

To observe these nerves a special method of dissection was necessary and I employed one differing somewhat from that of Hofmann. This method was comparatively simple with the aid of a small dissecting microscope. Very large frogs were used because their hearts were correspondingly large and thus easily operated upon. The pericardium was dissected away, and the heart completely removed from the body, when it was placed in Salt or Locke's solution. Here it would continue to pulsate for several hours, even though the solution were not warmed. A slit was made in the wall of the right auricle between the sinus and *bulbus aortæ*. Small hooks from which weights were suspended were attached to the edge of the slit, and served to widen the opening made. If several of these hooks were attached at convenient places and the tissue dissected between them, the right auricle could be completely spread out. This afforded an excellent view of the transparent septum with the left auricle behind it, and the sinus

to one side at the auricular margin. The ventricle was tilted so that one could look down upon the orifice. This allowed careful examination of each portion of the heart during the contraction (Fig. 1). The above procedure, as a rule, produced no harmful effect on the rhythmic movements of the heart, and one could experiment upon it at will.

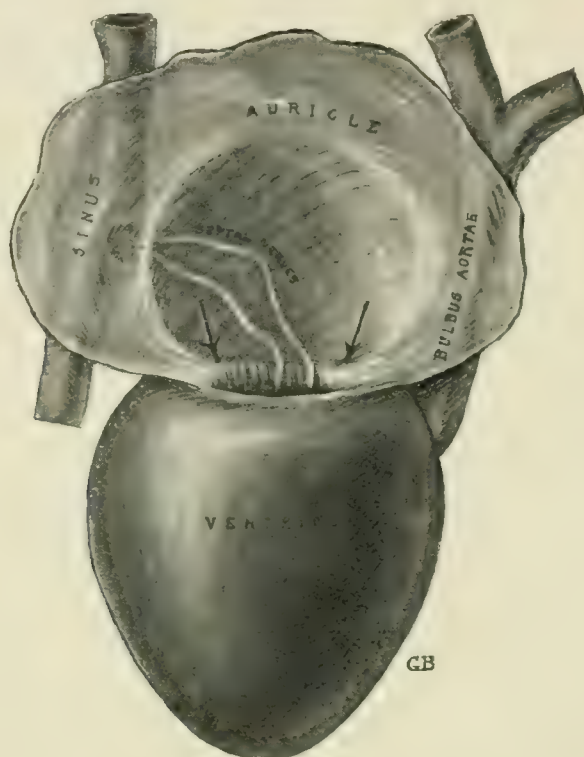


Fig. 1. Shows appearance of the frog's heart after dissection. Arrows point to auriculo-ventricular ring described.

This preparation also afforded an excellent means of studying the wave of contraction as it passed over the heart, since both the internal and external surfaces were exposed. The relationship which any part of the heart bore to any other could be very easily observed. I soon became interested in the musculature surrounding the auriculo-ventricular ring, and its relation to the conduction of the stimulus from auricle to ventricle. In hearts of slow rhythm that portion shows a definite contraction, distinctly separate from the contractions of either auricle or ventricle. It occupies the greater part of the time usually attributed to the pause which takes place at that point. A very slow rate brings out this interposed contraction very distinctly, and close observation shows a slight pause both before and after its movement. In hearts beating more rapidly it is impossible to separate the contraction of this ring from the general peristaltic-like wave which rapidly passes over the entire organ.

It was first suspected that this appearance might be due to a movement of the rudimentary valves, or to fling from the preceding auricular contraction. In the death of some hearts, however, all the other portions became still, leaving the ring contracting alone, which showed it to be a definite muscular action.



At the beginning of the experiments I attempted to obtain simultaneous graphic records of the various portions of the heart. None of those which were tried, however, were of sufficient delicacy to record the minute contraction of the ring. It was therefore necessary to be content with simple inspection of the changes which took place during the contraction of the heart, and in order to rule out the subjective errors of a single observer the phenomena were all demonstrated to and confirmed by Prof. L. F. Barker and Dr. A. D. Hirschfelder.

Histologically it has been shown by many writers that the auricles and ventricles have direct muscular connections. Kent<sup>8</sup> first demonstrated in some mammals that distinct muscle strands connected these two portions of the heart. Previous to this, however, Gaskell's work<sup>3 & 4</sup> had led him to believe that when the contraction wave reached the auriculo-ventricular junction it stimulated the ventricle to contraction. The most important findings were those of Wm. His, Jr..<sup>6</sup> He described a definite bundle of fibres passing from the auricles over the auriculo-ventricular junction to end in the ventricular musculature. His work was later confirmed by Retzer,<sup>15</sup> Tawara, and others, who added further details to the previous description. In the hearts of the lower animals we find structures of similar nature. McWilliam<sup>14</sup> describes a ring of muscle in the heart of the eel which surrounds the auriculo-ventricular junction. This ring is continuous on one side with the auricle, and on the other with the ventricle. Keith and Flack<sup>9</sup> have shown that there exists in the frog a similar ring around the base of the valves. Gaskell in experimenting on this ring in the frog found that excising any part of it had no effect on the sequence of the heart, but complete excision produced block.

These writers have all looked upon this portion of the musculature merely as a conducting system over which the stimulus passes to the ventricle. From their descriptions, however, it definitely coincides in location with the muscular ring described above. Therefore it would seem that this ring has a double action. First, it is a definite muscular entity with a distinct co-ordinated contraction in the heart sequence. Second, by means of its contraction it transmits the stimulus from the auricles to the ventricle. With this in mind we then see that the sequence in the frog's heart is made up of five distinct contractions.

The sinus, which acts as the pace-maker, contracts first; from this the stimulus spreads over the auricles, causing their contraction; then the auriculo-ventricular ring, ventricle, and *bulbus aortæ* contract successively, the action of one being completed before the next begins. There is still some doubt as to the path of stimulation from the sinus to the ventricle. McWilliam states that it passes both through the auricular tissue proper and the basilar portion of the auricle. Retzer, Keith and Flack, on the other hand, hold that the basal portion of the auricle alone is involved. Experiments with the frog heart preparation seem to indicate that, at least in the frog, the entire auricular tissue is capable of transmitting the stimulus.

Separating the auricles from the ventricle at any point so as to include the junction of the basilar portion of the auricle does not interfere with the sequence of contraction. This is true as long as a bridge of auricular tissue remains of sufficient size to conduct the stimulus. If the bridge is too narrow, partial or complete block occurs. In all instances the ring contracts before the ventricle, showing that the course of the stimulus at that point has not been changed. Another reason also supports this view. If the stimulus passes over a direct path between the sinus and ring one would expect an immediate response on the part of the latter. This is not the case, however, for the complete auricular contraction plus a slight pause following it is interposed between the contractions of the sinus and the ring.

Up to the present, the time that elapses between the contraction of the auricle and ventricle has been ascribed simply to the slowing of the stimulus in the auriculo-ventricular tissues. Many explanations have been given to account for this pause, because its duration is longer than is accounted for by the conduction time of either nerve or muscle. In studying the action of the ring, however, another factor is now apparent which affords a more simple explanation. We are dealing not with the conduction time but with the contraction time of heart muscle. The ring acts like all the other portions of the heart in that it first contracts before the succeeding part receives the stimulus.

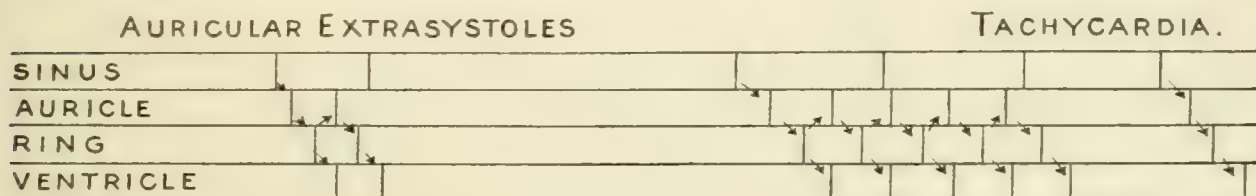
Many of the variations of auriculo-ventricular conduction can also be explained in the functional changes which the ring itself presents. It has a refractory phase, consequently any stimulus reaching it at that time will call forth no response, and we have an apparent block. Heat or any agent which increases the irritability of heart muscle causes an increase in the rapidity of the ring contraction. In this case the apparent conduction time from auricle to ventricle is shortened. Cold produces the opposite effect and we have a prolonged conduction time. The action of the ring of muscle in the various irregularities of the heart forms an interesting study. The preparation lends itself to this study very readily because the sequence can be so closely followed. The irregularities can be caused either by artificial stimulation or through the increased irritability of the heart muscle from the action of aconite (Cushny). The ring in most conditions serves as the "pace-maker" of the ventricle. Extrasystoles can be produced by stimulating the ring and these are followed by contractions of the ventricle. On the other hand, ventricular extrasystoles produced by stimulating portions of the ventricular surface are usually preceded by a ring contraction. In auricular extrasystoles, regardless of the point in which they may originate, the ring occupies the intermediate position in the sequence between the auricle and ventricle contraction.

Auriculo-ventricular block may occur at two points, either above or in the ring itself. If the supraventricular stimulus is checked at the auricular margin, the ring initiates a rhythm which the ventricle follows. Cessation of ring contraction occurs occasionally from various causes and here we have



an entirely different type of block. The stimulus from the auricle does not pass the auriculo-ventricular junction and the ventricle itself establishes its independent rhythm. This, however, is somewhat slower than that originating in the ring itself.

Retrograde rhythm may begin at either of two places : if it arises in the ventricle proper it is followed by the sequence ring, auricles and then sinus. It may originate, however, in the ring itself and the auricles and ventricle contract simultaneously. This corresponds very closely to that type of irregularity to which has been given the name "Nodal rhythm." \* Many auricular irregularities are also caused by this tendency of the ring to stimulate the auricle. I have frequently seen the types shown in the following diagram ; these were possibly due to a retrograde stimulus from the ring to the auricle.



The question of course immediately arises, were not these simply spontaneous auricular contractions, and not caused by a stimulation from the ring. In slow hearts, however, one could see the extra-auricular contraction arising at the auriculo-ventricular margin and spreading over the auricle. Another method which substantiates this consists in splitting the auricles longitudinally down to the auriculo-ventricular ring. One-half is attached to the sinus and ventricle ( $A^1$ ) ; the other is only connected to the auriculo-ventricular margin ( $A^2$ ). The contraction then runs as follows :

$S-A^1-R < \frac{A^2-R-V}{V}$ . This appears to be evidence that the auriculo-ventricular tissues may reverse the stimulus at that point. It would serve as a possible explanation for some of the extrasystoles and tachycardias arising in the lower segment of the auricles.

### Conclusions.

My observations permit of the following conclusions, which are intended to apply to the frog's heart :

A definite muscular structure connects the auricles with the ventricle and its contraction holds a fixed position in the sequence of the heart beat. This lends additional evidence towards the theory that the transmission of stimulus is through muscular rather than neural paths.

\* True initiation of the rhythm by the cells of the auriculo-ventricular bundle, not the absolute irregularity now known to be due to auricular fibrillation.

The conduction time at the auriculo-ventricular junction is accounted for by the contraction of the ring.

The ring usually serves as the pace-maker for the ventricle, but the latter is also capable of establishing its own rhythm when it receives no supraventricular stimulus.

The ring may stimulate either the auricles or the ventricle, and so be responsible for certain complex types of irregularity.

In conclusion I wish to express my thanks to Dr. Barker for many suggestions during the course of these experiments.

#### BIBLIOGRAPHY.

- <sup>1</sup> ADAM. *Archiv. f. d. ges. Physiol.*, Bonn, 1906, cxi, 607.
- <sup>2</sup> CUSHNY. *Heart*, Lond., 1909, i, 1.
- <sup>3</sup> GASKELL. *Journ. of Physiol.*, Lond., 1883, iv, 64.
- <sup>4</sup> GASKELL. *Schäfer's Textbook of Physiol.*, Lond., 1900, ii, 169.
- <sup>5</sup> HERING. *Archiv. f. d. ges. Physiol.*, Bonn, 1907, cxvi, 143.
- <sup>6</sup> HIS. *Centralbl. f. Physiol.*, 1895, ix, 469.
- <sup>7</sup> HOFMANN, F. B. *Archiv. f. d. ges. Physiol.*, Bonn, 1901, lxxxiv, 130.
- <sup>8</sup> KENT. *Journ. of Physiol.*, Lond., 1893, xiv, 233.
- <sup>9</sup> KEITH AND FLACK. *Journ. of Anat. and Physiol.*, Lond., 1907, xli, 172.
- <sup>10</sup> KEITH AND FLACK. *Lancet*, Lond., 1908, xlii, 1.
- <sup>11</sup> KREHL AND ROMBERG. *Zeitschr. f. Pathol. and Pharmakol.*, 1892, xxx, 49.
- <sup>12</sup> LEWIS. *Heart*, Lond., 1910, ii, 23.
- <sup>13</sup> MACKENZIE. "Diseases of the Heart," London, 1910.
- <sup>14</sup> McWILLIAM. *Journ. of Physiol.*, Lond., 1888, ix, 167.
- <sup>15</sup> RETZER. *Anat. Record*, Philad., 1908, ii, 149.
- <sup>16</sup> SCHÖNBERG. *Zeitschr. f. Pathol.*, Weisb., 1908, ii, 153.



# A DESCRIPTION OF A CASE OF COMPLETE HEART-BLOCK, INCLUDING THE POST-MORTEM EXAMINATION.

BY ALFRED E. COHN

(*From the Hospital of the Rockefeller Institute for Medical Research*),

AND

THOMAS LEWIS \*

(*From the Cardiographic Department, University College Hospital Medical School*).

A MINISTER, aged 77, who was a patient of Dr. C. E. McDade, was brought to University College Hospital Medical School in March, 1911, for electrocardiographic examination, through the kindness of Dr. H. Batty Shaw.

He had been under Dr. McDade's care for a number of years, and his condition was reported in the *Lancet*, 1906, ii, page 653.

The patient was an extremely hard working man who had had excellent health until 1904, when he was 70 years of age.† In July of that year and in February, 1905, he had attacks of vertigo and flatulence. In June, 1905, the pulse rate was noticed to be 40; the beats were strong and regular. He complained of easy exhaustion, especially after exertion. There was then no vertigo, and breathing was free and the urine normal. The heart sounds were clear. On June the 23rd, the pulse beat regularly at 78. From July the 7th to 14th, the pulse beat regularly at 40 and he was performing his usual arduous work without fatigue. On August the 13th, the pulse was regular at 63, and on November the 13th, regular at 38. On December the 15th he seemed to be failing in strength. The pulse was 32 and sometimes irregular. He took to bed on the 19th and the pulse became regular again, varying in rate from 28 to 32. At this time rapid oscillations of the jugular veins were seen. On January the 25th, 1906, a trace of albumen was found in the urine; the pulse remained slow. On February the 5th the rate was 63, the beats being regular. For the next four weeks it varied between 48 and 80. By March the 15th, 1906, the pulse rate was normal and active work was resumed in May.

The patient's condition remained satisfactory till October, 1907, when the pulse again fell to 40 and continued at or about this rate until May, 1908. Most of this period was spent in bed or indoors. Albuminurea was present at this time. There had been no further attacks of vertigo.

---

\* Working under the tenure of a Beit Memorial Fellowship.

† For these notes we are indebted to Dr. McDade and to his *Lancet* report.

From May to November, 1908, the pulse was normal and the albuminurea vanished, work being resumed. In November, 1908, the pulse rate fell to 37 and continued at or about the rate of 34 until death occurred in April, 1911. The albuminurea also reappeared and was maintained; moreover the feet and legs became swollen and this condition persisted. At this time the systolic blood pressure was measured at 220 mm. Hg..

On October the 22nd, 1910, a cough developed and strained him a good deal; and a few days later he had a fit of unconsciousness accompanied by lividity.

From January to March, 1911, feebleness increased. Oedema of the ankles and albuminurea were continuously present.

On March the 24th he came to University College Hospital Medical School. The curves, which are reproduced (Fig. 1) demonstrated complete heart-block; the auricular rate was 88 and the ventricular 34. The shape of the ventricular complexes in the three leads was such as is said to indicate hypertrophy of the left ventricle. At this time there was a good deal of breathlessness. With the exception of a systolic apical murmur, the sounds were normal.

In the morning of April the 5th, 1911, he complained of "stupid feelings" in the head; in the afternoon he became gradually comatose and died.

The post-mortem, which was performed by Dr. McDade, was limited to the heart and aorta. The latter were very atheromatous. The heart was fixed in Müller-Formol, as described in previous communications.

#### *Macroscopic anatomy of the heart.*

The ventricle measures 13 cm. anteriorly from the *A-V* groove to the apex and 11.5 cm. posteriorly. Its weight is 732 grammes.

On the surface of the heart, more especially over the right ventricle, there is a layer of more than the normal amount of fatty tissue. The pericardium in numerous places is thicker and whiter than normal. The right auricle is dilated a little and the endocardium is opaque. The *tænia terminalis* is not hypertrophied. The tricuspid valve admits four fingers easily; its edges are thickened. The cavity of the right ventricle is not enlarged. The muscle breaks easily under the finger. There are no ante-mortem dots in any of the chambers. Its wall measures 6 mm. at the base, and 6 mm. at the conus arteriosus. The *corpora Arantii* of the pulmonary valve are slightly thickened. The left auricle is considerably dilated; its endocardium is white, thick and smooth. The mitral valve admits three fingers in line. The edges are thick like those of the tricuspid valve. The aortic flap of the mitral valve shows advanced atheroma. The cavity of the left ventricle is slightly dilated, the dilatation being most prominent below the aorta in the outflow tract. The wall at the venous base measures 15 mm., at the level of the papillary muscles it measures 16 mm., and at the apex 10 mm. The trabeculæ are flattened. The endocardium over them is



smooth and thin, but that covering the membranous septum and the adjoining areas is very thick and firm. The corpora Arantii of the aortic cusps are thick and at their attached margins their density is cartilaginous : they were slightly incompetent in the fresh state. The anterior sinus of Valsalva, the line of attachment of the aortic cusp, is calcareous. The other sinuses of Valsalva present an advanced athero-sclerosis. Advanced athero-sclerosis is also found in the coronary arteries. The descending branch of the left coronary artery shows a calcareous plaque near its origin, and also farther along in the course of the vessel. Similar changes are found in the right coronary vessel. The lesions do not constrict the lumen of these vessels. There is no lesion at or near the septum membranaceum to indicate that the *A-V* system has been compromised. The foramen ovale is closed. Tissues were excised for microscopic examination:—(1) Two pieces of the wall of the left ventricle. (2) a block of tissue at the junction of the superior vena cava and the right auricular appendix, containing the sino-auricular node, (3) a block of tissue from the interventricular septum, containing the *A-V* node, main stem and the upper portions of the right and left branches of the *A-V* bundle.

#### *Microscopic examination.*

Pieces of tissue from the left ventricle show many connective tissue scars, in which the muscle fibres are either atrophic or destroyed.

*Sino-auricular node.*—This node is found in 2,140 sections. Of these 1,000 were cut 8 micra and 1,140 were 9 micra thick. The total length of this node is therefore 18,260 micra or 18.26 mm.. It lies 2 mm. from the pericardium. At the point where it is first seen, the superior vena cava has already joined the right auricular appendix, so that it begins below the level of the angle of this junction. Actually the superior vena cava still shows its complete lumen and it has not yet widened out into the cavity of the right auricle. The node therefore does not lie in the wall of the superior vena cava. In the upper portions it consists of little more than loose-meshed connective tissue which contains about a half-dozen thin and somewhat elongated muscle fibres. It is completely surrounded by fatty tissue. Large nerve trunks and a small vessel lie in its immediate neighbourhood. At a slightly lower level the node lies 1.5 mm. from the pericardium, measures 2.5 mm. from side to side, and extends for 1.5 mm. into the substance of the auricular wall. Its shape is roughly triangular. The pericardium over the node is thick. The size of the artery to the node has increased; the adventitia is hypertrophied. The various structures which form the node differ from the description usually given, because there is very little interlacement. Its muscle fibres sometimes contain vacuoles. At a still lower level, the vessels to the node, both artery and vein, are prominent and occupy the greater portion of its structure. Its position, size and shape remain unchanged. At its upper extremity it is almost completely surrounded by fatty tissue so that it has an island-like appearance. Farther down the

shape becomes more definitely triangular; it lies 2.5 mm. from the pericardium and measures 2.5 mm. from side to side, and is 3 mm. deep. The apex of this roughly triangular structure communicates freely with the auricular muscle. At a still lower level, the node is flatter and longer, the long diameter being parallel to the pericardium; it is 1 mm. deep and lies only 1.5 mm. from the pericardium. The tail, the lowest level of the node, is about 2 mm. from the pericardium and measures 1.5 mm. by 1.5 mm.; its shape is triangular as in the upper levels.

To sum up, the node is almost 2 cm. in length in the fixed state. It lies close under the pericardium through its whole extent. It is first seen at the angle where the superior vena cava joins the right auricular appendix, but it does not extend so high as to lie in the wall of the superior vena cava. Its shape above is first roughly triangular, but at lower levels it is flattened and elongated, while the tail is again triangular. The node is peculiar in that the amount of contained muscle tissue is small relative to the size of the entire structure and that the fibres interlace very little. There is a good deal of connective tissue, but the amount is within the limits of normal variation. It is also peculiar because it is isolated in so large a part of its length by fatty tissue. A feature of the artery to the node which is commented on by Oppenheimer is shown in this case. It consists of the presence of small bundles of muscle, arranged in longitudinal fashion, outside the inner circular layer of the media. The arrangement is similar to that seen in the central veins of the suprarenal gland.

*The auricular and ventricular septa.*—The cross section of the interauricular septum, the plane of the section being at right angles to the long axis of the heart, shows an unusual preponderance of fatty and connective tissues, over the muscle, which usually forms its substance. This change in relation is more apparent in the dorsal portions. In the interventricular septum numerous scars formed of dense connective tissue, some of which have undergone hyaline degeneration, are seen at all levels. In these scars, the muscle tissue is either atrophic or destroyed. The muscle fibres which form the interauricular septum vary a great deal in their diameter. Their nuclei are different in size and the perinuclear space is wide and free from muscle fibrils, so that the general appearance of the fibres suggests that of Purkinje cells. These fibres are neither grouped nor arranged in a specific order, so that it is impossible to attribute a separate function to them, as has been done. They represent a variety of muscle atrophy. The vessels of the septum, more especially the posterior coronary artery, show an advanced grade of athero-sclerosis. Advanced sclerosis is also seen at the root of the aorta, more especially in the sinus of Valsalva of the left posterior flap. In the corpus Arantii of one of the aortic cusps, cholestrin crystal spaces are seen. There is no evidence of recent inflammation.

*The auriculo-ventricular node* lies, as usual, to the right of the central fibrous body, it is very small, and is compressed laterally. It communicates



with the auricular muscle (the auriculo-nodal junction) by means of a well developed strand of muscle to the left, but by a much attenuated strand to the right. In the upper levels the relative size of these two strands is the reverse of the usual condition, but lower down it is normal. Between the two strands a mass of fatty tissue is found, continuous with the fatty tissue described in the interauricular septum. The auriculo-nodal junction and the auriculo-ventricular node itself are smaller than normal. The node is recognised mainly from its position. The fibres do not interlace in the usual fashion, they are coarser and do not show the normal number of nuclei. The artery commonly found in relation to the node is wanting. Near the node, however, a vessel is found, the structure of which, in contrast to that of the other arteries at this level, is normal. Thus, the continuity of the muscle structure from the auricle to the main stem of the *A-V* bundle, is maintained by a node which in appearance differs little from the auricular muscle. At the transition from the node to the *main stem* of the auriculo-ventricular bundle, there are masses of dense connective tissue. In addition to these there is much loose-meshed connective tissue separating the individual muscle fibres. A number of blood sinuses are also found. They consist of a single layer of endothelial cells surrounded by walls of dense connective tissue, free from muscle. They occupy a considerable portion of the bundle, while the number of muscle fibres is very much reduced. After a short course in the membranous septum, the main stem lies under the endocardium of the left ventricle. A portion of the fibres now passes dorsally and lies between the endocardium of the left ventricle and the lowermost portion of the central fibrous body. This branch, thin and small at its origin, spreads out later under the endocardium and comprises the left branch. At a lower level the mass of tissue forming it becomes greater. Compared with the left branch, the right branch is large, although the number of muscle fibres contained in it is relatively small. The pathological change, consisting of the old connective tissue and blood sinuses described in the main stem, is continued in the right branch to the lowest level examined. Here few muscle fibres are seen in it and the entire structure is very small. At this level the left branch is well developed and presents no abnormality. The smooth muscle fibres, which are described by Nagayo and which are found in the endocardium of the left ventricle and between it and the *A-V* system which lies in the outflow tract, is well developed. The fibres of the left branch show vacuoles. The difference in colour between the muscle of the conducting system and the myocardium is well seen in this case.

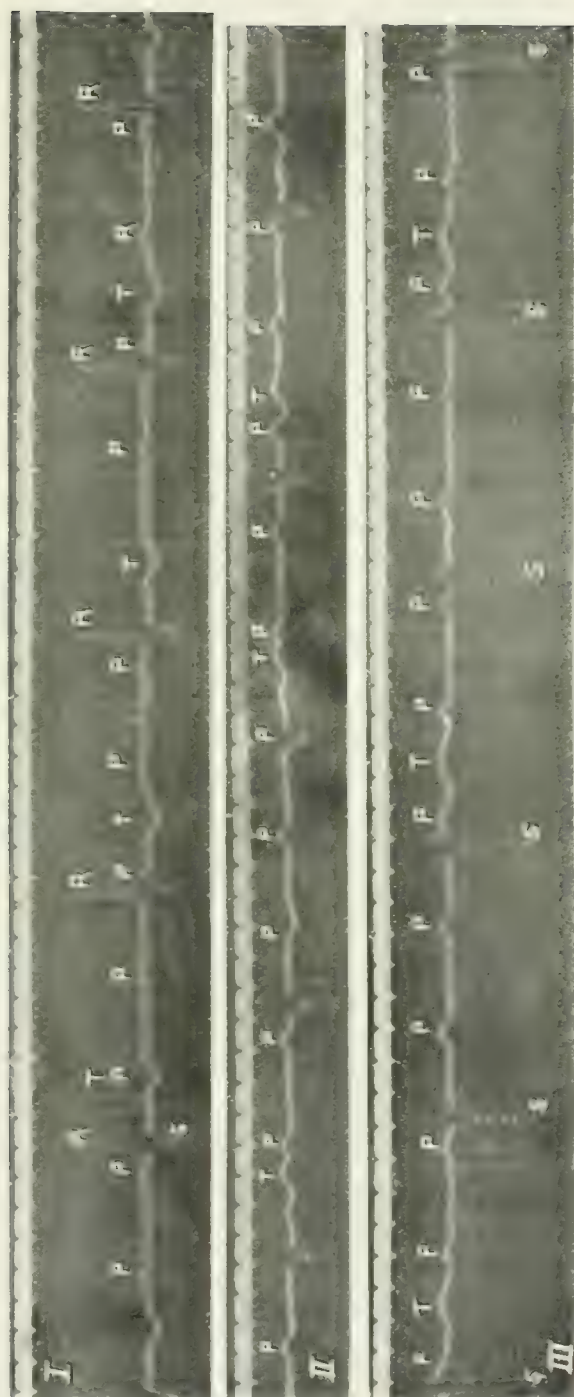
To sum up, in the conducting system of this heart the auricular nodal junction is smaller than usual. The auriculo-ventricular node is flattened and small and it is not characteristic either in the arrangement of its muscle or in the nature of its fibres. The main stem and the right branch show conspicuous pathological lesions. The lower portions of the right branch show that this structure is partially atrophic. The left branch is small above and larger below ; it presents no serious lesion. A complete transverse

lesion is therefore absent. The area of the muscle in the bundle, seen in the cross section, is seriously reduced by connective tissue formation and by the presence of the sinuses described. There is no evidence of an acute or subacute process. The lesions are manifestly chronic.

#### SUMMARY.

A case of Adams-Stokes' syndrome is described in which bradycardia occurred from time to time for nearly six years. An electrocardiographic examination thirteen days before death revealed complete heart-block. The patient died comatose; old inflammatory lesions were found which seriously compromised but did not completely divide the main stem and right branch of the auriculo-ventricular bundle.









# AURICULAR FIBRILLATION AND COMPLETE HEART-BLOCK. A DESCRIPTION OF A CASE OF ADAMS-STOKES' SYNDROME, INCLUDING THE POST-MORTEM EXAMINATION.

BY ALFRED E. COHN

(*From the Hospital of the Rockefeller Institute for Medical Research*),

AND

THOMAS LEWIS\*

(*From the Cardiographic Department, University College Hospital Medical School*).

## CLINICAL OBSERVATIONS.

THE history and the condition of the patient who forms the subject of this communication has been described in three previous articles. The original account is to be found in Mackenzie's paper.<sup>8</sup> More detailed accounts have been published by Lewis and Mack,<sup>7</sup> and by Lewis.<sup>6</sup>

It may be well briefly to recapitulate these reports.

M. M. was born in 1865; he contracted syphilis in 1887. In 1894, he had his first attack of syncope and had suffered from more or less prolonged attacks of loss of consciousness, sometimes accompanied by convulsions, up to the time when he was first examined. The first record of slow pulse rate dates from 1906, but his detailed history leaves little doubt that it had been present for a longer period.

He was seen by Dr. Mackenzie in November, 1908, when the first tracings were taken, and his pulse rate was then about 30 to the minute. He was under continuous observation from this time until the date of his death and was an inmate of a very large number of hospitals and infirmaries in London. The condition of the heart during the whole of the three years was almost constant. The ventricle generally beat quite regularly, at a rate of about 32 beats per minute, though from time to time the rhythm was disturbed by premature ventricular contractions. A total absence of any sign of co-ordinate auricular contraction throughout, and the replacement of these signs by those which, as we now know, characterise fibrillation of the auricle was a remarkable feature of the case.

The diagnostic features as they were summed up in the last report are as follows :—

### 1. *The evidence of complete heart-block.*

#### A. A history of syphilis.

---

\* Working under the tenure of a Beit Memorial Research Fellowship.

- B. The occurrence of fits accompanied by cessation of the ventricular action.
- C. The persistence of a slow ventricular action in the intervals, at rates known to be characteristic of an independent ventricular rhythm.
- D. The absence of compensatory pause after the premature ventricular beats.

2. *The evidence of auricular fibrillation.*

- A. The complete absence of *a* waves in the jugular curves in scores of observations.
- B. The complete absence of *P* variations in the electrocardiograms (Fig. 4).
- C. The presence of the characteristic oscillations of auricular fibrillation in the electrocardiograms (Fig. 4)\*; and, as may be now added, the occasional presence of rapid undulations in the venous curves during the diastoles.
- D. The determination that the electric oscillations were maximal when leads were taken directly from the chest wall, the electrodes being fixed in the vicinity of the right auricle.

It was upon this evidence that the conclusion was based that the two conditions, heart-block and auricular fibrillation were present in one and the same patient.

In regard to the general course of the patient's illness between 1908 and 1911, it is only necessary to state that apart from slow and progressive weakening, there was no change, and that abundant records of the pulse and venous curve were taken in Dr. Mackenzie's clinic up till the day preceding death.

*The nature of the terminal fits.*

The fits observed during the last days of the patient's illness were not dissimilar to those previously recorded, with the exception that no movements of the veins of the neck were seen during the long periods of asystole which accompanied them. They have been described for us by Dr. Silberberg to whom we are indebted for the following observations.

"The attacks of unconsciousness and the mild convulsions commenced at 5 o'clock on the morning of July the 6th, 1911. They ceased at 9 a.m., but returned at 11 a.m., and continued at short intervals till 1 p.m. . Between 1 p.m. and 2.30 p.m. he was free from them. From this hour until death occurred (the morning of the 8th) there was a similar repetition of relapse and recovery."

---

\* For the figures, reference should be made to the original descriptions.



"The attacks were of varying duration; lasting for a few seconds to twenty or thirty seconds. They were accompanied, one and all, by a lapse of the ventricular beats, readily observed at the prominent apex beat. The onset of unconsciousness was gradual, and the patient was aware of the impending attack, being conscious that his heart has temporarily ceased to beat. He became restless; he groaned and uttered words of complaint. In a few seconds he could not be roused, the eyes rolled upwards and deviated to the right: the pupils dilated fully, and the corneal reflex was lost. Cyanosis of the face, already present, deepened to lividity; the breathing became stertorous and air was sucked in vigorously, his cheeks sinking deeply between his edentulous gums. Much flatus was passed. After twenty seconds of unconsciousness, epileptiform manifestations appeared; the convulsions started in the face, the arms became rigid and spasmodic flexor movements appeared. The lower limbs showed no convulsive movements. A single beat of the heart, during the fit, lightened the degree of unconsciousness, two or three beats brought him to a dazed condition and, after a few more beats, he rapidly recovered, conversing rationally, though necessarily showing exhaustion. The first beat of the recovery was usually a weak one, the ensuing beats were more forcible. During the periods of comparative lucidity he complained of aching and sore feelings all over, more especially in the limbs. He was too feeble and exhausted to move. Pain, relieved by eructation, was present over the upper abdomen. On several occasions he vomited a pint or more of greenish fluid, an incident which seemed to afford relief."

The patient died in a fit on the morning of July the 8th. He became suddenly and deeply cyanosed, the face and arms showed the usual convulsive movements, but he failed to recover from the attack.

During the period of "status epilepticus," continuous tracings were taken by Dr. Silberberg from the apex beat. The rigidity of the arms and neck rendered further graphic record impossible; the ventricular pulsations were the only prominent movements. The whole length of a long curve of 21 minutes duration is included in the accompanying diagram (Fig. 1), in which each beat has been accurately placed; (the error is nowhere greater than one-twentieth of a second). The rate at any point may be calculated from the vertical lines which are separated by two-second intervals. Two strips of the actual curve are published as examples of the observations (Fig. 2 and 3).

The events which are portrayed in this diagram are of very considerable interest. The usual rate of the rhythm of the ventricle for this patient was 32 per minute. This rhythm appears from time to time in the chart, and the rate is either 30 per minute or somewhat less, namely 27; thus it is seen over the whole of the lines, *h*, *j*, *k*, *l*, and *m*, and over the greater part of line *e*. The rhythm is not quite regular, for premature beats appear from time to time. These beats are separated from those which precede them by a second or a little more or less; occasionally two or three premature beats

succeed each other (line *l* and line *d* directly after the pause), each following at about the same interval. From time to time they recur so frequently as to form a new rhythm, varying in rate from 60-80 per minute. It is the relation of these relative tachycardias to the periods of asystole which is so important. *The tachycardia, except where it is of brief duration, as in line "e," is invariably followed by a prolonged pause; and none of the prolonged pauses of the curve occur except immediately at the termination of a period of relative tachycardia.*

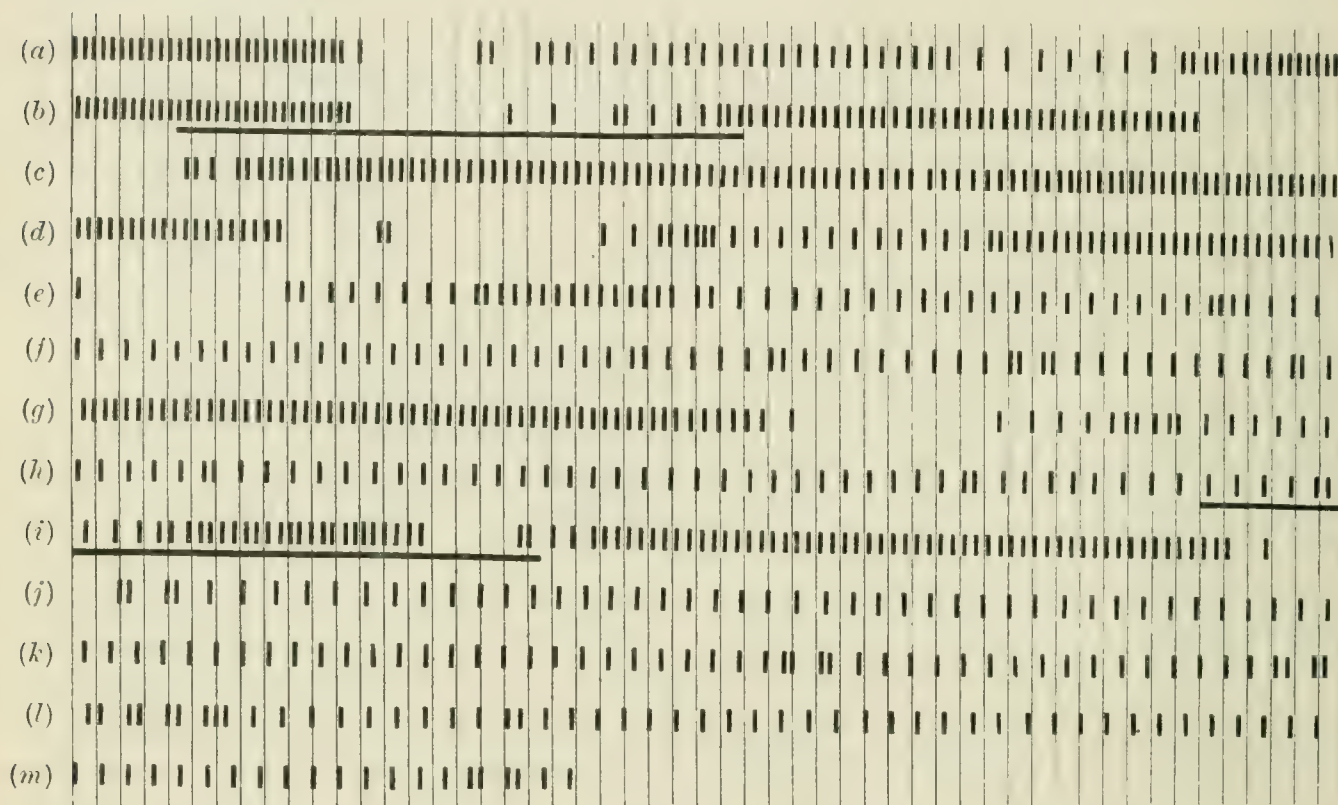


Fig. 1. A diagram compiled from a continuous curve of the apex beat, the duration of which was 21 minutes. The diagram reads from left to right, following consecutive lines. Each beat of the original curve has been charted on a large scale and the chart has been reduced subsequently photographically. The vertical lines are placed at two-second intervals. Two pieces of the original curve are reproduced in Fig. 2 and 3; the corresponding portions of the diagram are marked by means of heavy horizontal lines drawn beneath them. The relation of the (relative) tachycardial periods to the long asystolic intervals is very clearly shown.

The meaning of this phenomenon is quite clear. We have a clinical repetition of a phenomenon which has been studied experimentally and in detail by Erlanger and Hirschfelder.<sup>4</sup> When a slow ventricular rhythm is developed as a result of bundle section and a new and interrupting rhythm of faster rate is established, the new rhythm takes precedence to the old, and the latter passes into a condition of temporary abeyance. The cessation of the new rhythm is marked by a period during which physiological impulse formation in the ventricle is dormant and its awakening is gradual; hence the long pause which follows the ending of the new rhythm. The nature of the fits, and the underlying cause in this patient, is consequently apparent. The long asystole or "stoppage" as Erlanger has termed it, is brought about



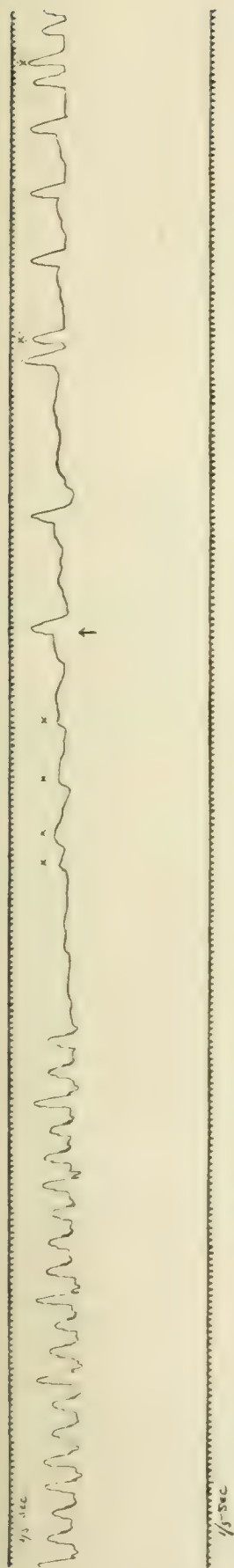


Fig. 2 and 3. Portions of the original curve from the apex beat. The time-marker is in one-fifth seconds.

Fig. 2 shows the termination of a period of relative tachycardia; it is followed by a pause of 13 seconds (the pause is interrupted by movements of the lever which were due to restlessness of the patient). The pause is followed by a slow but accelerating rhythm.

Fig. 3. Shows the commencement and termination of a short period of relative tachycardia; it commences in a premature beat and ends in a long pause of 8 seconds duration. Premature beats are marked by asterisks in the figures.

by an interference with the natural production of the idio-ventricular rhythm, as a result of the successive appearance of premature beats. In experiment the longest pause is generally followed by other pauses, which, though considerably longer than those which separate the beats of an established rhythm, are shorter than those which precede them. The same events are seen in this clinical case, though they are more irregular than are the experimental instances.

#### POST-MORTEM EXAMINATION.

The post-mortem was carried out by one of us at Mount Vernon Hospital on the 8th of July, 1911, a few hours after death. The body was that of a well developed and well nourished individual. Rigor mortis was present. There was slight œdema of the ankles. The conjunctivæ and skin had a yellowish tinge. An old and dense scar, 4 cm. in diameter, was noted above the right knee. Four other scars, each about 2 cm. in diameter and having a somewhat serrated margin, lay together over the left iliac crest. The external and internal jugular veins were a little dilated. The costal cartilages were not calcified.

#### *Macroscopic examination.*

The *tonsils* were fibrosed. The *tongue* and *palate* were normal. The mucous membranes of the *larynx* was yellow and thickened and showed some superficial petechiæ. The *trachea* contained a little frothy and bloodstained mucus. There were a number of dilated veins at the cardiac end of the

*oesophagus.* The *stomach* was more dilated than normal and its mucous membrane was deeply congested. The *intestines* and colon were not distended. The mucous membrane was injected.

The *pleurae.* On the right side, a transverse shelf of very strong adhesions, between diaphragm and parietal pleura, isolated the lower 12 cm. of the cavity. The lung lay entirely above it, but the space communicated with the main cavity by a small aperture in front. Isolated, thin but strong adhesions united the lung and parietal pleura; they were thicker and more numerous at the apex and along the posterior margin. No fluid was found in the sac. On the left side and on a level with the heart, the lung was not visible from the front. The whole pleural space was obliterated by soft, spongy adhesions resembling connective tissue.

The *pericardium.* The pericardium was bound to the two pleural membranes, and to the chest wall in front, by soft adhesions of a character similar to those found in the left pleura. When fully exposed and viewed from the front, the pericardial sac and its contents filled the whole of the lower portion of the left pleural cavity. At the level of the fourth interspace, the right margin lay 7.5 cm. from the middle line. At the level of the sixth cartilage, the margin lay 11.5 cm. from the middle line. The apex lay in the anterior axillary line in the sixth interspace. The pericardial cavity was completely obliterated by abundant adhesions; the two layers were fairly readily separable. The adhesions were firmer over the right auricle, and especially along the line of the sulcus terminalis, but the entire surface of the pericardium was roughened by the adhesions, which were old and dense. From the *A-V* groove to the apex along the anterior interventricular groove, the ventricle measured 16 cm. A similar measurement on the posterior surface was 12.5 cm.. The width of the heart along the posterior *A-V* groove was 13 cm.. The right ventricle occupied the greater part of the anterior surface.

The *heart.* The heart weighed 899 grammes. The surface of the heart-presented a considerable increase of fat deposit. The fat around the auriculoventricular groove was oedematous. There was little or no blood in the ventricles, but there was an excess of it in the great veins and auricles. The right auricle showed extreme dilatation, more especially the right auricular appendix. The cavity was about the size of a closed man's fist. The *tænia terminalis* in its upper extremity was hypertrophied, as were also the *musculi pectinati*, but the posterior wall of the right auricle was very thin. The endocardium was whiter than normal and seemed to be especially thickened below the orifice of the coronary sinus.

The tricuspid ring measured 13 cm. in circumference and readily admitted four fingers in line. The edges of the valve were slightly thickened but not hardened, and apart from slight matting together, showed no abnormality.

The right ventricle was slightly dilated. Its walls and trabeculae were hypertrophied. The muscle was brown, soft, coarse and friable. The wall measured 9 mm. at the base at the right border, 4 mm. at the apex, and 6 mm.



at the conus arteriosus. On the trabeculæ and more especially at their origins and points of division there were irregularly shaped oval and linear thickenings of the endocardium. They were cream coloured, dense in consistency and circumscribed. These were elevated as much as 2 mm. above the surrounding surface and were from 1 to 2.5 cm. in length. On the endocardium of the conus arteriosus, 15 mm. from the pulmonary valve there were areas of a similar nature but more extensive, one measuring 20 and another 25 mm. in length. Their outline was very irregular. The cusps of the pulmonary valve were fenestrated and the *corpora-Arantii* were slightly thickened.

The left auricular appendix was bound down by adhesions and was noticeably smaller than the right. It measured 3.8 cm. as opposed to 8 cm. for the right, the measurement being made from the middle of the *tænia terminalis* to its apex. The wall of the auricle was dilated and moderately hypertrophied; it measured 6 mm.. The endocardium was white and thick, but smooth. The mitral ring admitted three fingers in line. The edges of the mitral valve were thickened and smooth and not hardened. In the attached margins there were no calcareous deposits.

The wall of the left ventricle was dilated and hypertrophied and measured 17 mm. at the base, 22 mm. at the level of the papillary muscles and 9 mm. at the apex. The outflow tract below the root of the aorta was dilated. The wall of the left ventricle was thin at the left border, measuring only 5 mm., 4 cm. above the apex. On this portion of the surface of the heart, the adhesions were very dense. The main branch of the coronary artery to this portion of the heart was not occluded. In places there were yellowish streaks in the muscle. Elsewhere there were numerous scars. The enlarged papillary muscles showed white subendothelial nebulæ. The endocardium was smooth on the whole, but moulded on the trabeculæ and also at their junctions, cream coloured plaques were found like those in the right ventricle. They were more numerous on the left side. The posterior aspect of the posterior papillary muscle was entirely encased by such material. In the outflow tract, directly under the anterior portion of the membranous septum, a similar thickening was found, elevated 2 mm. above the level of the endocardium, and measuring 1 × 2 cm.. The other plaques of similar nature varied in length from a few millimetres to several centimetres. No calcareous deposits could be felt in or about the septum membranaceum. At the upper portion of the left ventricle, at the level of the A-V ring and at the right half of the cavity was an *intracardial aneurysm*. Its exact position (Fig. 5), was to the right of and behind the junction of the two flaps of the mitral valve and consequently to the left of and below the origin of the aortic valve, more especially its right posterior cusp. The aneurysm was shaped like a portion of a sphere. Its diameter was 33 mm.. The posterior wall of the aneurysm was formed by the posterior wall of the ventricle, and its level was that of the coronary sinus. The coronary sinus was compressed from before backwards but its lumen was not compromised, while the branches of the

coronary artery, though small, were not occluded. The right wall of the aneurysm was formed by the septum between the left ventricle and right auricle and corresponded in part to the insertion of the mesial flap of the tricuspid valve. The wall of the aneurysm was calcareous but smooth and showed no thrombi. Pressure in the aneurysm was directed backwards, upwards and to the right and was exerted on the end and the opening of the coronary sinus, and also on the septum between the two sides of the heart so that this was protruded into the cavity of the right auricle (see Fig. 5). The involved area corresponded, when seen from the right auricle, to the wall lying between the opening of the coronary sinus and the septum membranaceum. It is just in this situation that the auriculo-ventricular node and the beginning of conduction system is usually found. It was presumed that the aneurysm might have damaged these structures. Examination of Fig. 8 will show that this was not the case.

The lunulæ of the aortic valve were thickened and so were the *corpora Arantii*, but the valve presented no other abnormality. There was some atheroma in the sinuses of the *Valsalva*. Atheroma and athero-sclerotic patches were found along the course of the coronary arteries. These did not seriously narrow the lumina of the vessels anywhere. The foramen ovale was closed.

The *arteries*. The pulmonary artery showed occasional atheromatous patches and was pinkish-yellow in colour. The thoracic aorta was bile-stained, the endothelium seemed to be a little œdematous and there were scattered patches of atheroma. The abdominal aorta was extensively degenerated. Atheroma was advanced; œdema and ulceration were present. The coronary arteries presented little thickening; the coronary sinus and the cavities of the heart were free of ante-mortem clot.

The *lungs*. The right lung weighed 560 grammes, the left 525. The tissue was deeply pigmented, emphysematous and a little œdematous. Otherwise these organs were normal. The bronchial lymph nodes were black. Neither these nor the mediastinal nodes were enlarged or fibrosed.

The *liver* weighed 1,236 grammes. It was small and very hard. A number of firm, isolated adhesions united it to the diaphragm. The surface was irregular and showed a mild degree of hobnailing. One or two large superficial scars were present. The section was mottled red and greenish-yellow. The red areas were depressed. Fine, pink trabeculæ of fibrous tissue were clearly visible throughout large areas of the organ. The tissue was very tough. Glisson's capsules seemed more fibrous than usual. The liver appeared to be fatty, fibrous, congested and somewhat bile stained. The gall bladder was small and the wall was thick.

The *spleen* weighed 640 grammes. The surface was adherent to the diaphragm in several places. A number of small, irregularly shaped, cream-white masses were present on the surface and projected from it. The organ retained its shape. The section was dark, the tissue tough; the Malpighian capsules were not prominent. There seemed to be an increase of fibrous tissue.



The *pancreas* was larger than normal and consisted chiefly of mottled pink and yellow areas, in which the gland substance could be traced only from place to place.

The *kidneys* weighed 176 and 192 grammes respectively. The capsules were non-adherent. Apart from the conspicuousness of the glomeruli and slight general congestion and increased firmness, they seemed to be normal.

The *suprarenals* appeared to be normal. The cortex was dark brown, and the medullary substance light grey.

The *testicles*. Both tunicae vaginales contained about a drachm of yellow fluid. On the right side the testicle was normal, and there was a varicocœle. The left testicle was small and fibrosed.

The *peritoneum* was smooth. There was about a half-pint of yellow fluid in the cavity.

The *brain*. The calvarium was normal. The pia-arachnoid membrane was œdematous; the superficial veins were congested. The basal and cortical arteries were normal. The brain showed no abnormality on section. The venous sinuses were empty.

The *vagus and sympathetic nerves* presented no abnormality.

#### *Microscopic examination.*

All the pieces excised for microscopic examination were fixed in Müller-formol (9 : 1). The heart, medulla oblongata, pons and vagus nerves were fixed in the same fluid. The technique of examination of the heart was the same as that used and already described in this *Journal*.<sup>1</sup> On account of the difficulty which would have been experienced in cutting sections of the septum of the heart with the aneurysm in place, it was decided to shell out this structure. This proceeding was accomplished successfully. No incisions were necessary; blunt dissection sufficed to enucleate it in one piece. The description given below (see Fig. 5) will show that no injury whatever was sustained by the structures of interest in this study. The following tissues were excised for examination :—

- (1) The cavo-auricular junction, bearing the sino-auricular node.
- (2) A portion of the septum between the two halves of the heart, bearing the auriculo-ventricular node, main stem and branches.
- (3) A piece of the left ventricle.
- (4) Four pieces of the aorta, two thoracic and two abdominal.
- (5) Two pieces of the liver.
- (6) A piece of the pancreas.
- (7) A piece of the spleen.
- (8) Two pieces of the kidney.
- (9) The medulla oblongata and pons Varolii.
- (10) The two vagus nerves.

The *cavo-auricular junction, bearing the sino auricular node*. A piece of the superior vena cava was left attached so that Wenckebach's bundle could be examined. Apart from the changes which occurred in the cardiac muscle fibres in this case, no pathological lesions were found. The amount of connective tissue was not greater than elsewhere and there was no evidence of acute inflammation. The muscle fibres throughout those portions of the heart examined were much larger than normal. There was no fragmentation of the muscle and no granular degeneration. The transverse striation was clear and the nuclei well stained. In many of the muscle fibres there was an unusually large space about the nucleus which was clear of muscle fibrils, so that they resembled Purkinje cells. They had no definite arrangement, and were so scattered as to make it impossible to regard them as forming a system. The spaces about the nuclei contained no pigment. The nuclei themselves varied very much in size and shape, but for the most part they were much larger than normal. Their margins were usually irregular and the distribution of chromatin was uneven. Here, as elsewhere throughout the heart, connective tissue of a loose areolar nature was increased between the fibres and numerous scars of connective tissue were found. The smaller blood vessels were abnormal. The adventitia was but little thickened but there was thickening of the muscle of the media. The position of the internal elastic membrane showed an increased amount of connective tissue which sometimes extended into the intima. In a few places, loose connective tissue was seen invading the media from the adventitia. Vacuoles appeared frequently in the muscle fibres of the vessels. The intima was hyperplastic in many places, and the lumen often seriously reduced in diameter. A few small vessels were found to be occluded and others presented but a slit-like channel. The elastic tissue throughout the heart stained poorly or not at all, and was in marked contrast to that found in the kidney of the same case, which was used as a control.

The sino-auricular node was seen at a level below that at which the cavo-auricular junction was formed. The angle of junction lay, in fact, 3 mm. above the upper extremity of the node.\* The node could not be said to lie in the wall of the superior vena cava. At the anatomical junction between the superior vena cava and the auricle, there was complete separation of the muscular systems of both by fat and by some connective tissue. It was in this fatty tissue that the node was first seen, lying much nearer the vena cava than the auricle but quite separate from it. From its upper extremity to its end, it measured 21.55 mm., the measurement being computed from the thickness of the sections multiplied by the number in which it was found. The upper extremity of the node lay, as has been said, nearer the superior vena cava, while a little lower down it was situated nearer the auricular muscle. It was found close to the pericardium throughout, except

---

\* Koch<sup>5</sup> has shown that in the hearts of dogs, an extension of the sino-auricular node reaches 2 mm. upward on the wall of the superior vena cava, but that the node can be recognised 0.75 to 1 mm. above the cavo-auricular angle.



at its upper extremity. Here it was 3.5 mm. from the surface, but a little lower (1.5 mm.), it was 1.5 mm. deep and maintained this depth (0.75 to 1.5 mm.) throughout its extent. The shape of the node varied constantly in its course. In its highest level it was roughly triangular, the apex of the triangle pointing toward the pericardium. A little further down, the node was circular (Fig. 6). But the greater portion of it (66%) had an elongated shape, the long axis in cross section being parallel to the pericardium (Fig. 7). The greatest length of this long axis was 5.5 mm. and its width at the corresponding level varied from 1.0 to 0.25 (See Table I).

TABLE I.

|       |     |       | DEPTH.   | LENGTH. WIDTH |        |          |
|-------|-----|-------|----------|---------------|--------|----------|
| Slide | 122 | .. .. | 3.5 mm.  | .. ..         | 0.75   | 1.5 mm.  |
| ..    | 134 | .. .. | 2.0 mm.  | .. ..         | 1.00 × | 3.0 mm.  |
| ..    | 141 | .. .. | mm.      | .. ..         | 1.00   | 2.0 mm.  |
| ..    | 155 | .. .. | 1.5 mm.  | .. ..         | 2.00   | 2.0 mm.  |
| ..    | 181 | .. .. | 1.0 mm.  | .. ..         | 2.00 × | 1.0 mm.  |
| ..    | 199 | .. .. | 1.0 mm.  | .. ..         | 2.00 × | 1.0 m.m. |
| ..    | 226 | .. .. | 1.0 mm.  | .. ..         | 1.50 × | 1.5 mm.  |
| ..    | 257 | .. .. | 1.0 mm.  | .. ..         | 1.50 × | 1.5 mm.  |
| ..    | 284 | .. .. | 1.0 mm.  | .. ..         | 2.50 × | 1.0 mm.  |
| ..    | 292 | .. .. | 0.75 mm. | .. ..         | 3.00 × | 1.0 mm.  |
| ..    | 310 | .. .. | 0.75 mm. | .. ..         | 4.50 × | 0.5 mm.  |
| ..    | 324 | .. .. | 0.75 mm. | .. ..         | 5.00 × | 0.5 mm.  |
| ..    | 344 | .. .. | 0.75 mm. | .. ..         | 5.50 × | 0.5 mm.  |
| ..    | 351 | .. .. | 1.00 mm. | .. ..         | 5.50   | mm.      |
| ..    | 358 | .. .. | 1.00 mm. | .. ..         | 3.0 ×  | 0.25 mm. |
| ..    | 364 | .. .. | 1.00 mm. | .. ..         | 3.5 ×  | 0.5 mm.  |
| ..    | 384 | .. .. | 1.25 mm. | .. ..         | 3.0 ×  | 0.25 mm. |
| ..    | 393 | .. .. | 1.50 mm. | .. ..         | 2.25 × | 0.25 mm. |
| ..    | 402 | .. .. |          | .. ..         | 1.50   | mm.      |
| ..    | 416 | .. .. | 1.50 mm. | .. ..         | 0.50   | mm.      |

The upper third of the node was entirely destroyed by connective tissue. This was dense and probably old (Fig. 6). Fat tissue occupied the area at the sides of the node, between it and the pericardium, and was also found within its structure. Except in one or two places, where there were round cells, there was no evidence of a recent or acute inflammation. Below this level, that is, in the lower two thirds, muscle tissue appeared in the node and rapidly increased in amount, but the amount of connective tissue was probably always more than normal (Fig. 7). The increasing amount of muscle tissue occurred at the anterior portion of the node, while the posterior portion remained quite sclerosed. The node was at almost every level in direct relation with nerve trunks. Ganglia were found, as were also nerves which contained ganglion cells. About some of these there was dense connective tissue. The node contained an artery and in some sections two. In some parts of its course, the artery showed a distinct endarteritis. A small artery at one level was entirely occluded and canalized.

*The auriculo-ventricular system.* A block of tissue, including the interauricular and interventricular septum, was excised. The upper margin ran parallel with the upper edges of the aortic cusps, the lower margin was

parallel with this, two to three centimetres below the membranous septum ; the anterior margin was at the anterior extremity of the septum, and the posterior margin was the posterior wall of the heart itself. The sections were cut parallel with the upper margin. The entire site of the aneurysm already described was included in the block. The bed of the aneurysm was found to be a connective tissue structure, of a dense fibrous nature, which looked old. In a few places near the wall there were collections of lymphocytes. This was the only evidence of recent or acute inflammation. The bed of the aneurysm, which was also the inter-auricular septum (see Fig. 5 and 8), was very much thinned, convex towards the right auricle and contained no muscular tissue. The entire septum was consequently converted into a wall composed of fibrous tissue. Examination showed that the removal of the calcareous portion of the aneurysmal sac had involved the loss of no structure necessary for this study. The septum contained no muscular structures between the coronary sinus behind and the central fibrous body in front. Muscle fibres survived above the level of the aneurysm rather high above the auriculo-ventricular groove, but they did not descend to the auriculo-ventricular node. There was consequently no connection between the auricular muscle and the node ; the auriculo-nodal junction did not exist. Except for the muscle tissue of the auriculo-ventricular system, to be described presently, the entire interauricular and inter-ventricular septum in the neighbourhood of the aneurysm, the central fibrous body and the septum membranaceum were replaced by dense old connective tissue, poor in nuclei ; and in some places, notably in the posterior wall of the heart and at the root of the aorta, by fatty tissue. That portion of the interventricular septum in which the upper portions of the right and left branches of the conducting system are usually found, was also replaced, for 2 cm. anterior to the membranous septum, by connective tissue of the kind described. Muscle tissue was seen only in the lower parts of the block. In the sections the coronary sinus was seen to be compressed from before backwards. That wall of the sinus which was directed toward the cavity of the auricle contained a thick layer of loose connective tissue. The cardiac muscle tissue in this situation was thinned and was infiltrated with large amounts of dense connective tissue. A number of vessels were compressed and showed advanced endarteritis to the point of occlusion.

The auriculo-nodal junction, as has been said, did not exist. The node was, however, a well developed structure and showed the familiar interlacing arrangement. It followed the usual appearance of this structure also in the number, shape and size of the nuclei, the fineness of the fibres and the arrangement of the fibrous tissue. It was a normal node. At one portion a few small, dense masses of connective tissue were present but they did not appear sufficient in size or number to be considered pathological. The artery to the node appeared in the lower regions only. Its adventitia was thick and there was much connective tissue in the intima. At still lower levels the lumen was contracted on account of endarteritis. Passing forward from the



node (Fig. 8), the main stem of the *A-V* bundle progressed normally through the septum membranaceum for about 2 mm. when it ceased suddenly in the dense connective tissue of the septum already described. About 3 mm. farther along, the main stem was again identified. A hiatus of about 3 mm. was thus caused between the *A-V* node and the main stem, in the upper portion; of about 7 mm. at the lower; and of 12 mm. at the lowest level. The main stem was then followed through the septum membranaceum about 3 mm. Its anterior end was terminated by the dense connective tissue of which the septum ventriculorum was composed. The division of the main stem into the right and left branches was nowhere seen. This portion of the system, as well as the origin of the branches, was completely destroyed by the sclerotic process. The right branch was not identified at lower levels, but the left branch was clearly seen 6 mm. below the point at which the main stem disappeared. The failure to identify the right branch was due, no doubt, to the fact that the right half of the interventricular septum was sclerotic at levels lower than the left half. The left branch of the bundle did not partake of the hypertrophy of the rest of the heart. The nuclei of the conduction fibres were slightly irregular but the change from the normal shape and structures was much less than that seen in the intrinsic cardiac muscle. The distinctiveness of the nuclei of the conducting muscle was recognised here as well as in other hearts. The endocardium which lay over the left branch was especially thick, the thickening being due to fibrous changes in the lining membrane of the heart. The smooth muscle of the endocardium showed a normal development.

The *aorta*. The cusps of the sinuses of *Valsalva* were sclerotic, and this sclerosis involved the junction of the cusps especially. The aortic wall contained an increased amount of connective tissue. The thoracic aorta showed moderate thickening of the intima, the elastic tissue of which was hyperplastic. The medial layer was practically normal. Occasionally large plaques of the intima occurred, which showed degenerated and oedematous loose fibrillar connective tissue. They contained no calcium, cholesterin, or debris. The abdominal aorta showed areas where there were lymphocytic and rarely leucocytic collections in the intima. In a few places the media where it adjoined the intima was degenerated. Here the nuclei were not stained and the tissue looked hyaline. Elsewhere the media showed an increased amount of connective tissue. The intima was unequally thickened and showed distinct plaques. The plaques were hyaline, non-cellular, and in a few, large collections of needle-like vacuoles were seen, which in the recent state had been occupied by cholesterin crystals. In other portions of the intima there were cellular elements, lymphocytes, leucocytes and plasma cells. There was no deposit of calcium. Another section showed necrotic plaques which were in a pre-ulcerative stage. Here the degenerative changes in the media were more advanced, in that the nuclei did not stain and the tissue had assumed a hyaline appearance.

The *liver*. The capsule was very thick and in places shaggy. The thickening was for the most part due to an increased amount of fibrillar connective tissue, of normal appearance. In other places the thickening was due either to destruction or to partial atrophy of the underlying liver cells. The central veins were dilated, the surrounding liver cells were atrophic, and in many there was advanced fatty degeneration. A number of these cells showed brown pigment. In these areas a number of acini were compressed. The capsules of Glisson were normal.

The *pancreas*. There was increased interstitial fatty tissue and also some increase in the amount of connective tissue.

The *spleen*. The capsule was much thickened by dense masses of connective tissue. The substance of the gland was congested: and there appeared to be more than the normal amount of lymphatic tissue in it.

The *kidneys*. The glomeruli were distinctly more congested than were other parts of the organ. Adjoining the capsule, there were a number of small areas containing lymphocytes and others where there was an increase of connective tissue. The vessels were normal. There was a hyperplasia of the internal elastic membrane, probably normal at this period of life.

The *medulla oblongata* showed no abnormality. It was examined in serial sections.

The *right vagus nerve* showed no abnormality. Many ganglia were seen incorporated in its course. A small nerve (presumably the sympathetic) was seen running parallel with the vagus, into the interstitial tissue of which a hæmorrhage had taken place. The *left vagus* was like the right and in the section a small nerve containing a hæmorrhage was also seen.

*Summary*.—(1) The medulla oblongata showed no gross lesion. The vagus nerves were normal, but parallel with each nerve there was a small one containing a hæmorrhage. (2) The heart was hypertrophied in all its cavities. There was an aneurysm in the right upper portion of the left ventricle. There was partial sclerosis of the septum ventriculorum and complete sclerosis of the septum membranaceum. The myocardium contained numerous scars. There was practically no acute inflammation. The sino-auricular node was in part destroyed, being replaced by connective tissue. The main stem of the auriculo-ventricular bundle was divided from the auriculo-ventricular node by sclerotic tissue; and the distal end of the main stem, its point of division and the upper parts of both branches were destroyed by the same process. The arteries of the heart showed hypertrophy of the media, degeneration of their muscle fibres, and hyperplasia of the intima causing either partial (the more common lesion) or complete obliteration of the lumina. The aorta showed athero-sclerosis. (3) The liver showed chronic congestion, as did also the spleen, pancreas and kidneys.



## RELATION OF LESIONS AND HEART MECHANISM.

We do not propose to discuss the question of auricular fibrillation and its morbid anatomy at any length. The findings in this case, the partial destruction of the sino-auricular node and the scattered fibrosis in the auricle, conform with those which have been found by a number of other writers.

The case was remarkable clinically for the presence of definite signs of auricular fibrillation, while *the ventricular action instead of being rapid and irregular, as is usual in such cases, was slow and regular.* The opinion was held, and is still held, that a regular action of the ventricle is never associated with auricular fibrillation, except when complete functional dissociation of auricle and ventricle, so far as conduction is concerned, is present; and it was felt that as the ventricular action was persistently slow and regular, a lesion accounting for this action would be found, which was comparable to the lesions discovered at autopsy when ordinary dissociation of auricular and ventricular rhythms occurs. This expectation has been fully realised by the examination of the heart in this unique case. Complete division of the junctional system occurred at two levels at least. The post-mortem findings confirm the conclusion that if, in a case of auricular fibrillation, the action of the ventricle is regular, there is complete functional separation of the two chambers, so far as the conduction of impulses is concerned. The case is, so far as we know, the only one of its kind which has been recorded.

But there is another matter in connection with it of considerable interest. The post-mortem examination shows a lesion at the division of the bundle, and *destruction of the upper ends of both the branches.* Now when there is a single lesion of the main stem, the electrocardiogram of the ventricle retains its original form, consisting of the normal *Q, R, S* and *T*, or *R, S*



Fig. 4. (Reproduced from *Heart*, Vol. 1, p. 306, Fig. 18). An electrocardiogram, showing auricular fibrillation and the slow and peculiar ventricular beats which are considered to be associated with the action of a heart, in which both bundle branches have been destroyed. Note the duration of *S*. The time marker is in one-fifth seconds.

and *T* variations. When one or other branch is divided, anomalous electrocardiograms are produced, which as Eppinger, Rothberger and Stoerk<sup>2 & 3</sup> have shown, are distinctive of the lesions in question. In this clinical instance both branches were destroyed and it might be anticipated that, as a result, the ventricular electrocardiogram would be considerably modified. One of the original curves is shown in Fig. 4; it was taken

from lead *II*. Two ventricular beats are seen ; *R* is small, *S* is deep and *T* is tall, but the chief feature of the curve is *the breadth of "S."* The total duration, from the commencement of *R* to the end of *S* is approximately one-fifth of a second.

There is but one published electrocardiogram from an experiment in which both bundle branches had been cut. It is given by Eppinger and Rothberger<sup>2</sup> (Fig. 8 of their paper). The curve is almost identical with that now published ; *R* is short, *S* is deep and *T* is full ; but again the chief feature is the duration of *S*. The clinical and pathological observations are thus in the most complete accord. It seems from the comparison that division of both branches of the bundle may be diagnosed clinically.

#### SUMMARY.

1. The pathological report of a patient previously described as exhibiting auricular fibrillation and complete heart-block is now given. Complete division of the bundle was found, and lesions compatible with auricular fibrillation were seen.

2. The observations support a former conclusion that, when auricular fibrillation is associated clinically with a regular action of the ventricle, impulse conduction from auricle to ventricle is in abeyance.

3. A lesion is also described which divided both branches from the main stem of the bundle and from each other ; the electrocardiograms were of the form seen by Eppinger and Rothberger to follow a similar experimental lesion.

4. The lesions in the heart were of syphilitic origin and included a septal aneurism pointing from the left towards the right side, *i.e.*, from the direction of greater to that of lesser pressure.

5. The patient was the subject of syncopal attacks. The nature of the heart pauses, responsible for the attacks, has been shown. They followed periods of relative tachycardia, resulting from new impulse formation in the ventricle. This observation is exactly parallel to the experimental findings of Erlanger and Hirschfelder.

#### BIBLIOGRAPHY.

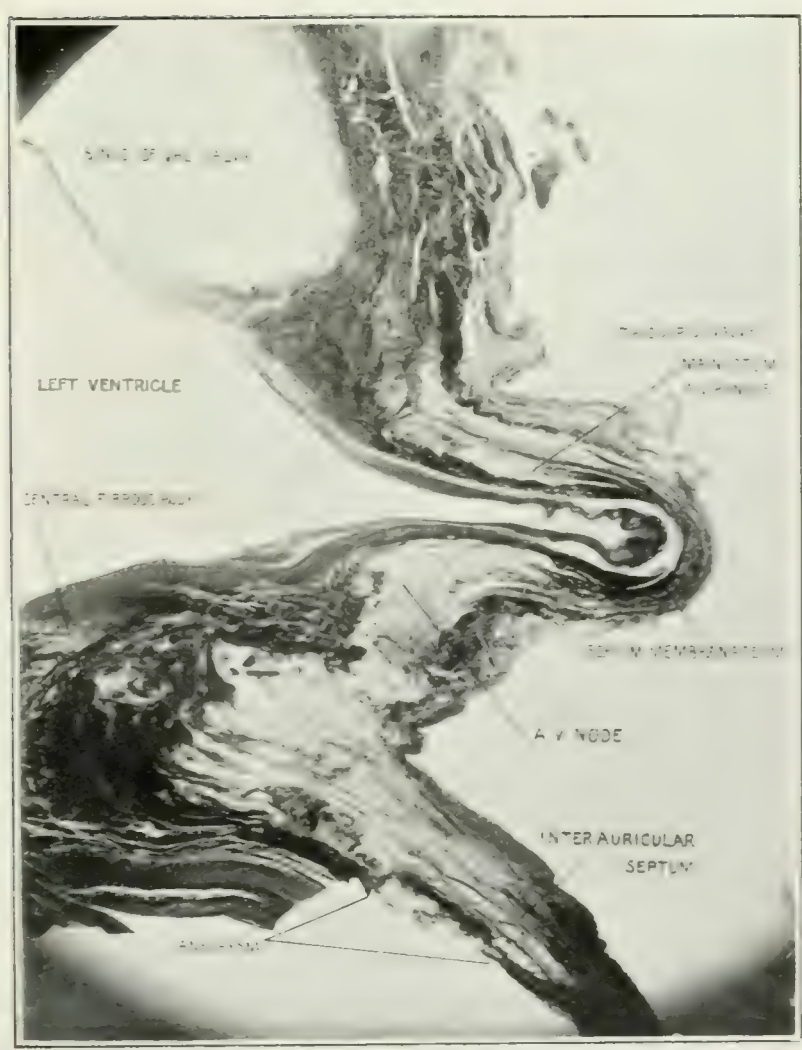
- <sup>1</sup> COHN, HOLMES AND LEWIS. *Heart*, 1910-11, ii, 241-248.
- <sup>2</sup> EPPINGER AND ROTHBERGER. *Zeitschr. f. klin. Med.*, 1910, LXX, 1.
- <sup>3</sup> EPPINGER AND STOERK. *Zeitschr. f. klin. Med.*, 1910, LXXI, 157.
- <sup>4</sup> ERLANGER AND HIRSCHFELDER. *Amer. Journ. of Physiol.*, 1905-6, xv, 153.
- <sup>5</sup> KOCH. *Med. Klinik*, 1911, vii, 447.
- <sup>6</sup> LEWIS. *Heart*, 1909-10, i, 351 ; case 13.
- <sup>7</sup> LEWIS AND MACK. *Quart. Journ. of Med.*, 1909-10, iii, 273.
- <sup>8</sup> MACKENZIE. *Heart*, 1909-10, i, 33 ; case 4.

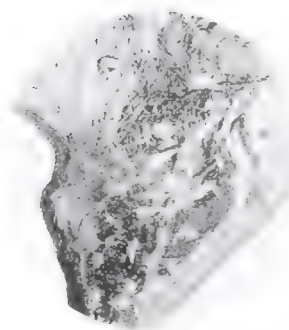
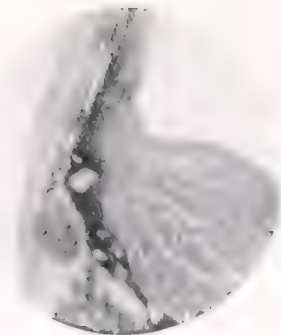


Fig.  
Fig.  
Fig.  
Fig.



FIG. 7.







## THE ACTION OF DIGITALIS IN THERAPEUTICS.

BY A. R. CUSHNY, H. F. MARRIS AND M. D. SILBERBERG.

*(From the Heart Wards of Mount Vernon Hospital and the Pharmacological Department of University College, London.)*

WHEN Withering<sup>20</sup> introduced digitalis into therapeutics as a remedy for dropsy, he also recognised that "it has a power over the motion of the heart to a degree yet unobserved in any other medicine and that this power may be converted to salutary ends." But he did not connect this cardiac action with the relief of dropsy, and Ferriar<sup>5</sup> first showed the relation and pointed out that "the power of reducing the pulse is the true characteristic" while "its diuretic power is a less constant and less essential quality of the plant." This reduction in the rate of the pulse led to the view that digitalis is a cardiac sedative, which appears to have been widely held about 1800, though Beddoes<sup>1</sup> and Kinglake<sup>7</sup> pointed out that while the pulse is slowed it is also strengthened, Beddoes demonstrating this by means of an instrument of the nature of a sphygmograph and maintaining that "in a certain dose digitalis will increase the activity of the arterial system." But the obvious feature of slowness of the pulse appears to have appealed more to the clinicians, and for many years the view prevailed that digitalis is a "sedative" to the circulation, which it slows and renders more feeble. Thus Pereira<sup>11</sup> recommends it in aneurism and hæmorrhages in order "to reduce the force and velocity of the circulation," placing it in the same category as repeated blood-letting and low diet for this purpose. This clinical view was supported by the experiments of Traube,<sup>17</sup> who showed that digitalis injected intravenously in animals slows the pulse by stimulating the vagus centre, and who appears to have ignored entirely the early clinical view that the circulation is strengthened and accelerated by digitalis. The action of digitalis on the heart apart from the inhibitory slowing was first demonstrated by Schmiedeberg<sup>14</sup> on the frog's heart, and has been generally recognised, although the attention of clinicians is still apt to be directed rather to the slowing of the pulse, which can be readily recognised and measured, than to the other features of the action.

One of us<sup>3</sup> demonstrated that in mammals small doses of the digitalis bodies injected intravenously slows the heart by stimulation of the inhibitory centre and at the same time strengthens the contractions and often lessens the relaxation of the heart by direct action on the cardiac muscle. The net effect is to increase the outflow of blood from the heart. Larger quantities reduce the efficiency of the heart by still further slowing its rhythm and thus

diminishing the total output. These views have been generally accepted, but it is still disputed whether the therapeutic effects of digitalis and its allies are to be attributed to the inhibitory action or to its direct cardiac action. In favour of the former it is often argued that by lengthening the inactive phase of the cycle more time is allowed the heart to recuperate its energy, and it is further a matter of common observation that the improvement of the symptoms under digitalis often is coincident with the slowing of the pulse.

The newer methods of clinical observation in heart disease seemed to promise to throw some light on this disputed question in therapeutics, and one of us has been engaged for several years in working on the problem with Dr. James Mackenzie in the Heart wards of Mount Vernon Hospital.\* It is hardly necessary to add that without his active interest and co-operation it would have been impossible to carry out the work.

Many of our investigations were performed with standardised tincture of digitalis, some with the tinctures of strophanthus and squills or with strophanthin put up in ampoules for us by Burroughs and Welcome, who state that it was isolated by them from specially selected and tested seeds of *Strophanthus Kombé*.

The actions of digitalis, strophanthus and squills† on the human heart were practically identical in our observations, though they may differ in some minor details, so that we have felt justified in treating the results obtained from one of them as applicable to the group. The disadvantages which attend the use of all three in the doses which are employed arise from the alimentary tract, and our first attempt was to discover some remedy which while inducing the therapeutic effects would have less gastric action, as in some cases we found it impossible to obtain the cardiac action of digitalis owing to the headache, nausea and vomiting which it induced.

It was hoped that an inhibitory action similar to that of digitalis might be induced by the use of aconite, which is generally reputed to slow the pulse in man, and which in large doses in animals stimulates the inhibitory centre in the same way as digitalis, while it is devoid of direct action on the heart muscle unless still larger doses are given. A number of cases were therefore treated with aconite and aconitine in a variety of doses, but Price<sup>13</sup> could elicit no slowing of the pulse in cases in which digitalis subsequently or previously had been effective, and this method of approaching the problem therefore broke down. On the other hand, helleborein injected in animals has the same effects on the cardiac muscle as digitalis, while it is practically

---

\* Some of our cases were reported by Silberberg. *Trans. roy. Soc. of Med. (Pharm. and therap. Section)*, 1911, May 16, p. 192, and the details of these have been omitted in the following pages.

† Squills has been in constant use in medicine for over 2,000 years, while digitalis has a history of only about 135 years and strophanthus of only 35 years. Yet the action of squills on the heart has only been recognised in the last half century, although some of the older physicians (*e.g.*, Home, *Clinical Experiments*, 1783, p. 387) observed that when large doses were used to cause vomiting the pulse was sometimes reduced in frequency, even to forty per minute.



devoid of action on the inhibitory centre. It thus seemed possible that in man the direct cardiac effects of the digitalis type might be elicited by helleborein, without concomitant inhibition. But this also failed, for helleborein given by the mouth even in half-grain doses had no demonstrable effect in heart disease, but often induced diarrhœa, which prevented its further use. This is probably due to its being absorbed from the bowel with great difficulty like the saponins with which it is nearly allied: apparently it never reaches the heart in sufficient quantity to elicit its characteristic action unless it is injected intravenously. Both these attempts to induce the effects of one side of the digitalis action thus proved abortive.

Another method of distinguishing between the two factors in the action of digitalis was thus adopted and proved more successful. If the inhibitory factor could be eliminated under digitalis without abolishing the therapeutic effects, then it would be proved that these are not dependent on the inhibitory action, but on the direct action on the cardiac muscle. The inhibition can be removed by the use of atropine, and we have therefore given atropine in a number of cases which were under the influence of digitalis. This can be done without any inconvenience to the patient, in fact we were repeatedly assured that the breathing was easier for some hours after the atropine injection. Atropine sulphate in dilute solution was injected in the forearm. Tracings of the radial pulse or of the apex beat were taken before the injection and were continued afterwards for one or more hours. The rate of the pulse given throughout this paper was taken from polygraph tracings, some of these being continued for many hours without interruption.

There is normally in man an inhibitory tone which slows the heart and which is removed by atropine, and this alkaloid therefore accelerates the pulse. The question to be determined was whether the digitalis slowing was an exaggeration of this inhibition: in this case atropine would accelerate the pulse not only to the rate prevailing before the digitalis was given but to the rate attained by the heart released from control by atropine before the digitalis treatment was instituted. It was therefore necessary to ascertain the rate of the released heart before the digitalis was given as well as after treatment was instituted, and for this reason at least two injections of atropine were requisite, one given during the digitalis treatment and one before it or after it had ceased.

It will be convenient to divide the cases into two groups, those in which the normal sequence of the heart movements was preserved except for some minor aberrations, and those in which the dominant feature was the fibrillation of the auricles. The effects of digitalis are much more satisfactory in the second class of cases and in particular the slowing of the pulse is a more marked feature in the effects as a general rule, as Mackenzie<sup>9</sup> pointed out in 1905 and has recently described in detail.

### I. NON-FIBRILLATING CASES.

Digitalis reduces the rate of the heart in a certain proportion of these cases and improves the general symptoms, such as dropsy. In most of the

instances in which the pulse is slowed, if the treatment with large doses be continued, partial heart-block or marked sinus arrhythmia is developed. Thus in seven cases out of twenty-one which Mackenzie<sup>9</sup> describes as "normal rhythm," the pulse was slow under digitalis, and in six of the seven either partial block or sinus irregularity was developed. As yet we have examined under atropine only those cases of normal rhythm in which there was definite slowing.

*CASE 1.\** C.O., male, aged 16. Admitted on October the 20th, 1910, when he was found to be suffering from mitral and aortic disease accompanied by shortness of breath, pain in the left chest and oedema. The pulse was regular and full, rate 138 per minute. The area of heart dulness was enlarged, the liver swollen and pulsating and crepitations were present at the bases of the lungs.

Digitalis improved the symptoms but induced heart-block and later vomiting. These disappeared when digitalis was stopped but returned when it was resumed. The *a-c* interval was not prolonged, when the rhythm was regular.

On December the 7th he had been without drugs for thirteen days. His pulse was 120 to 124 and regular. Atropine 1.50 gr. was injected hypodermically and raised the pulse rate to 130-133, an increase of 9 per minute.

On December the 19th he had taken 9 dr. of tincture of digitalis (20 m. t.d.s., in nine days), and heart-block and some phases of pulsus alternans were present. The ventricular rate varied from 72 to 84 per minute. Atropine 1.50 gr. was injected, and in seven minutes the regular rhythm returned, the block and pulsus alternans disappeared, and the rate increased to 112-116 per minute. The rhythm remained regular for two and a quarter hours and then the slowing due to digitalis heart-block returned. Increase in rate, 36 per minute under atropine.

*Summary.* Partial heart-block and slight pulsus alternans from digitalis were removed by atropine. The rate of the released heart was somewhat slower after digitalis than before its administration.

*CASE 2.* C.L., labourer, aged 45. Admitted July the 14th, 1911, complaining of stabbing pain in lower sternal region, sometimes shooting into left shoulder and back of neck and head, which is aggravated after exertion. Some dyspnoea after exertion. Occasional "thumping" of heart. During the last month some swelling of the feet observed and later swelling of abdomen. On examination some tenderness was detected over the sternomastoid and pectoralis muscles on the left side, and slight emphysema. There was no oedema, the heart sounds were normal and the pulse was regular at 64-72 per minute with very slight sinus arrhythmia. Blood pressure 110. After rest in bed for ten days there was no change in rate. On July the 26th an injection of 1.50 gr. atropine reduced the pulse from 70-72 to 66-67 at first, and after 20 minutes it rose to 74-75. A further injection of 1.50 gr. increased the rate to 83 and then to 86-89 and the sinus arrhythmia disappeared. Tincture of digitalis was ordered, 20 m. t.d.s. for 15 days; latterly slight nausea and constipation were induced, and the patient complained of a dull heavy feeling under the sternum. No headache. Blood pressure rose to 125-130. Pulse 62 per minute, regular, except for sinus slowing which was more marked than before treatment. Before digitalis exertion caused an acceleration from 68-78. After digitalis the acceleration was from 62 to 70 after exertion and occasional auricular extrasystoles were present. The injection of 1.50 grain atropine first slowed the pulse and then accelerated it to 78-80, and the sinus arrhythmia disappeared.

*Summary.* A regular heart, was accelerated by atropine to the usual extent. Digitalis caused slowing with some increase in the sinus slowing. Atropine accelerated the pulse to almost the same degree as before digitalis and removed the sinus slowing.

*CASE 3.* L.R., male, aged 66. Emphysema. Complains of shortness of breath on exertion, increasing recently. Suffered from rheumatism last four years, formerly from epilepsy. Admitted July the 13th, 1911.

---

\* For clinical details see *CASE 8*, cited by Silberberg.



Heart regular except for slight sinus arrhythmia, chest emphysematous, no murmurs, no excessive arterio-sclerosis for his age. Blood pressure 153-160 from day to day. Pulse rate 72. After rest in bed for 12 days no apparent change except less dyspnoea. July the 25th atropine 1/25 gr. raised pulse rate from 66 to 72-74 and abolished sinus arrhythmia. Put on digitalis m. 20 t.d.s.. July the 29th complained of headache and on the 30th vomited. Digitalis stopped on the 30th. On August the 1st, the polygraph showed after exertion a bigeminal pulse apparently from auricular extrasystoles and marked sinus arrhythmia independent of respiration (Fig. 2). There was a tendency to periodic respiration under digitalis which was not present before treatment and disappeared after digitalis was given up, but reappeared when digitalis was again instituted. On August the 2nd the bigeminal pulse was present even when the patient was at rest. 1/25 gr. atropine after preliminary slowing raised pulse from 57-58 per minute to 66-67. The sinus arrhythmia and the auricular extrasystoles disappeared (Fig. 1).

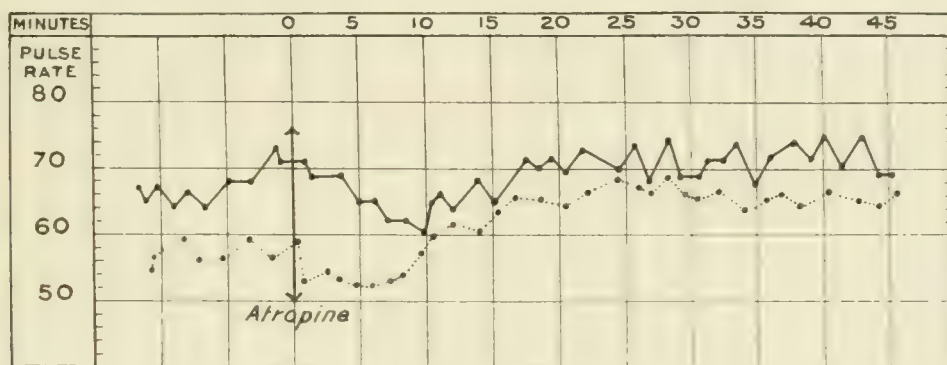


Fig 1.

Fig 1. (CASE 3). Chart\* of pulse rate under atropine. July the 25th before digitalis ———. August the 2nd after five days digitalis treatment ..... .

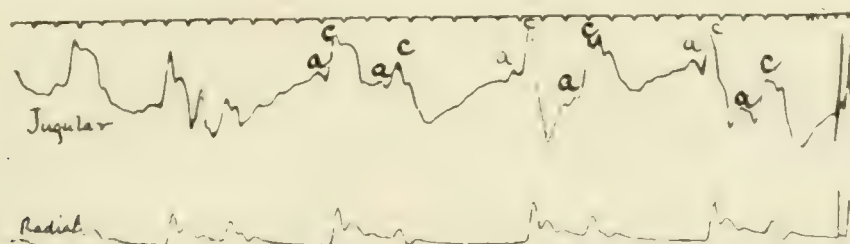


Fig. 2. (CASE 3.) Under digitalis. Auricular extrasystoles.

*Summary.* Digitalis slowed the heart, increased the sinus slowing and induced occasional auricular extrasystoles. Atropine accelerated the pulse to almost the same rate as that observed in the released heart before digitalis and removed the sinus arrhythmia and extrasystoles. Under digitalis this patient exhibited a tendency to periodic respiration.

**CASE 4.** L.W.† (Fig. 3), aged 21, waitress. Admitted complaining of pain over the heart and shortness of breath during the last five weeks. History of rheumatic fever. Area of heart dulness enlarged, mitral and aortic systolic and diastolic murmurs. Pulse, 99-100, regular. Blood pressure, 108-112. Tincture of digitalis, 20 m. t.d.s., induced nausea after 10 days, and soon afterwards the pulse fell to 60-70 and was irregular from heart-block. When digitalis was stopped the pulse rate rose to 96-100. Her P-R interval is 0.28 second (normal 0.12-0.17 second).

On April the 5th in the stage of digitalis heart-block (12 dr. taken), atropine (1/50 gr.) was administered. Eight minutes after there were phases of regular rhythm mixed with phases of irregular pulse, rate 79-86. In twelve minutes the rhythm was regular, and for eight minutes remained so at a rate varying from 104-110, and thereafter till the end of the observation there were again phases of regular and irregular rhythms. Dryness of the throat was complained of twenty minutes after the injection. Increase in pulse rate from 60-64 to 110-114 = 50.

\* In these charts the rate is indicated in the ordinates, the time along the abscissa.

† The earlier part of this case given by Silberberg (CASE 9).

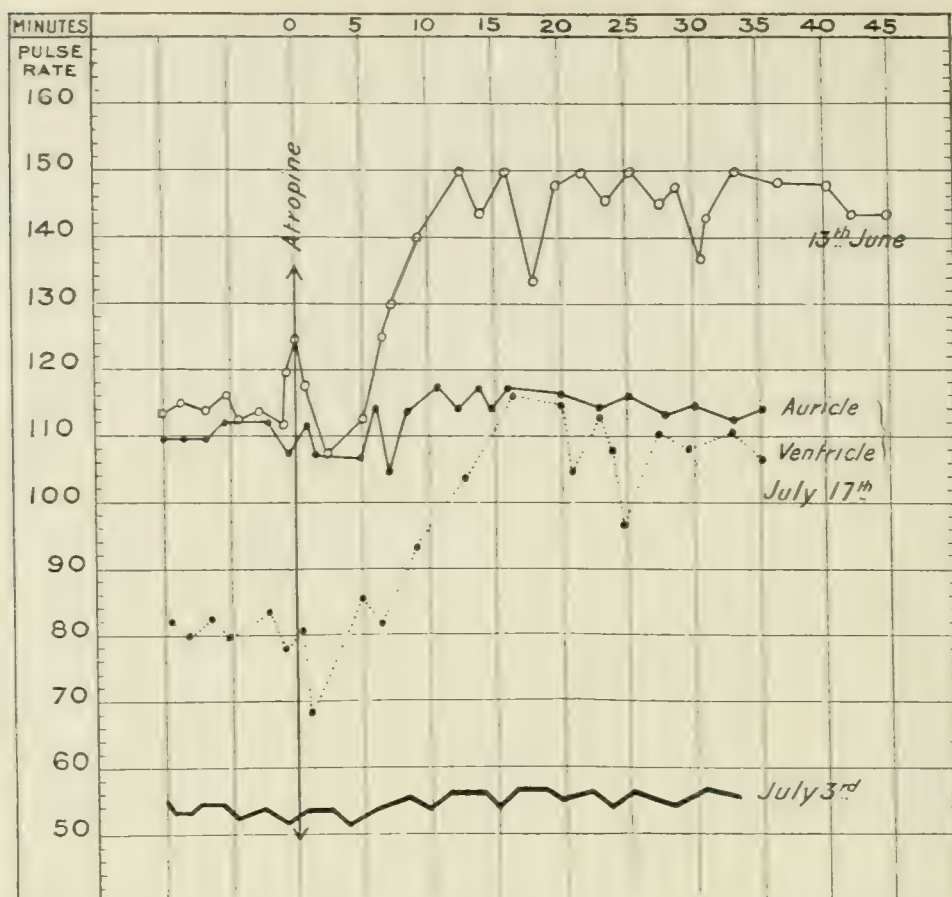


Fig 3

Fig. 3. Chart of pulse rate in CASE 4, under atropine. June the 13th, without digitalis o—o—o. July the 3rd under full digitalis (half-rhythm) ———. July the 17th, recovering from digitalis, half-rhythm frequently but not continuously. Auricle rate— ——. Ventricle— ·····.

On April the 25th the heart had reverted to its former rhythm of 90-100 per minute, and tincture of strophanthus was given, m. 20 t.d.s., and later 30 m. t.d.s. (47 dr. altogether) without inducing any change in rate or rhythm or any toxic symptoms. Treatment was stopped on June the 7th. On June the 13th the pulse was examined under atropine (1/50 gr.) (Fig. 3), and rose from 110-115 to 145-150 per minute and the slight sinus arrhythmia disappeared. On June the 20th tincture digitalis m. 20 t.d.s. was ordered, but the pulse remained unchanged in rate until the 29th when it was 65-75 and tracings showed periods of 2:1 heart-block alternating with periods of regular rhythm. The patient felt stronger and less breathless until the 27th when she began to complain of heaviness under the sternum, breathlessness and "thumping of her heart." On July the 1st these symptoms were more marked and she complained of nausea and sleeplessness. The pulse was now regular at 53-55 and tracings showed constant 2:1 heart-block. On July the 3rd these symptoms continued unchanged. The pulse was not quickened on exertion, while previously there had been some rise, e.g., from 90-110. 1/50 gr. atropine was injected and induced dryness of the throat and wide dilatation of the pupils, but had practically no effect on the rate of the pulse, except removal of very slight sinus arrhythmia (see Fig. 3). This result was so strikingly different from that obtained from the same patient on April the 5th that it was twice repeated on the following days with 1/25 gr. of atropine with the same result, practically no acceleration of the pulse. Digitalis was discontinued on July the 7th when severe headache, nausea and vomiting were present. The pulse began to quicken on July the 15th and on the 17th was 82, while the auricle was 110. Injection of 1/50 gr. atropine increased the rate of the auricle to 118 and the pulse from 82 to 118 for some minutes, the block disappearing entirely. Occasional ventricle contractions then began to fall out (Fig. 3). On the 18th the toxic symptoms were gone and the block had disappeared, but could be restored by pressure over the vagus in the neck, by exertion and by swallowing cold water. On July the 25th this had also disappeared and the rate was now 110-120, regular. On the 29th the dyspnoea returned. On August the 1st tincture digitalis m. 10 t.d.s. was ordered. On August 15th general condition was improved, pulse 90, regular, and block could be induced on vagal pressure or exertion. The dose was reduced to m. 10 b.d.s. and she was discharged and remains fairly well up to the present under this treatment. The blood pressure remained fairly constant at 125-135 throughout except during the full action of digitalis when it reached 140-145 mm. for a few days.



*Summary.* Digitalis caused partial heart-block, which when moderate in degree was removed by 1/50 gr. atropine, but when more marked (constant 2 : 1 rhythm) was unaltered by atropine. The rate of the auricle was hardly changed by digitalis except that a very slight sinus arrhythmia was noted before the block developed. In the later phases (July the 3rd) there was less sinus slowing. In each case atropine removed this minor irregularity. In the earlier stages of block where series of beats at 1 : 1 alternated with other series of 2 : 1, the change from 2 : 1 to 1 : 1 was generally preceded by a few beats in which sinus slowing was very marked. This slowing of the whole heart appeared to allow time for the bundle to recover from exhaustion and it then remained capable of carrying each impulse from the auricle for some time. Exhaustion was then induced by the rhythm and it fell back on the 2 : 1 rhythm until again it was allowed time for recovery by a sinus slowing. Atropine removed this sinus slowing with the block. Before digitalis was given, atropine induced a considerable rise in the pulse rate, which indicates that the pacemaker was controlled by tonic activity of the inhibitory mechanism. After digitalis, this control was less, for the rise in the auricular rate was smaller. The rate of discharge of the pacemaker remained practically the same.

*CASE 5.* R.W., male, aged 35, hairdresser. Smoked moderately and has latterly been drinking. He had pneumonia 18 months ago and has never been well since. In March, 1911, he observed swelling of the feet and abdomen, which responded to treatment. He has been nervous and shaky ever since then. Admitted July the 21st, 1911.

Complains of nervousness and tightness across chest. Colour good. Some emphysema and a little œdema at base of lungs. Heart extended to  $4\frac{3}{4}$  inches to left of middle line. No localised impulse. First sound seemed feeble; no murmurs. Pulse was 60, and apart from moderate sinus arrhythmia and full a-c interval (0.2 secs.), was regular in character. The sinus arrhythmia continued when the breath was held. Blood pressure, 150. Vessels were soft and showed no signs of degeneration. No precordial tenderness was present and the liver was not enlarged or tender. Some œdema of legs. No albumen in urine which amounted to 20-30 oz. Ordered rest in bed. On July the 31st he had lost all his subjective symptoms. Pulse 60, blood pressure 140, lungs clear, and no tenderness anywhere. Pulse rate on exertion quickened from 62 to 72. Atropine (1/50 gr.) injected hypodermically on July the 28th (Fig. 4) caused initial slowing of the

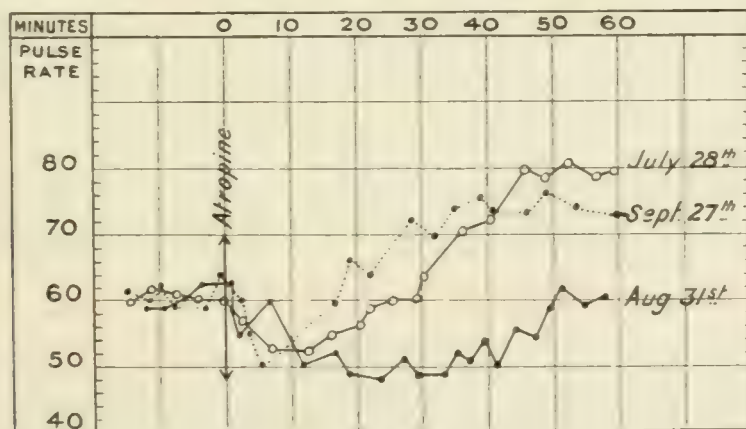


Fig 4.

Fig. 4. Chart of pulse rate of CASE 5 under atropine. July the 28th before digitalis, o—o—o. August the 31st under digitalis, ———. September the 27th after the digitalis effects had passed off ———.

pulse followed by acceleration to 78-80 from the normal 60-62, and the sinus arrhythmia disappeared. On August the 3rd ordered tincture digitalis m. 20 t.d.s. On August the 8th

(after 5 dr. digitalis) sinus arrhythmia increased and some auricular extrasystoles were present after exertion. August the 14th (after 13 dr. digitalis) there was marked slowing of whole heart, the pauses being sometimes almost double the length of the preceding pulse interval, suggesting some form of block above the auricle. On August the 19th he complained of specks before his eyes and precordial distress. On August the 24th an electrocardiogram kindly taken for us by Dr. Lewis showed frequent pauses of auricle and ventricle (Fig. 5), the duration of the pause being exactly double the interval between the ordinary *P* waves, again suggesting block above the auricle. The *P-R* interval was short after each pause and then lengthened to about 0.2 secs. in the next cycles but was not abnormally lengthened in any beat. The polygraph records showed this irregularity, but in addition there was unmistakable auriculo-ventricular block (Fig. 6). On August the 29th 1/50 gr. atropine caused the usual slowing followed by no acceleration, the pulse remaining at 60-62. The sinus irregularity was quite unaffected. August the 31st 1/25 gr. atropine induced dryness of the throat and other symptoms but did not accelerate the heart or render it more regular, both forms of slowing persisting unchanged (Fig. 4). September the 7th headache complained of and digitalis was stopped. On September the 27th the irregularities had disappeared and he had reverted to his original condition. Atropine (1/50 gr.) accelerated the pulse from 60-62 to 73-76 (Fig. 4). On September the 28th digitalis was resumed. October the 2nd arrhythmia present during the secondary slowing after exertion, not present during rest. October the 4th arrhythmia permanent except that it disappears on exertion with the acceleration of the pulse.

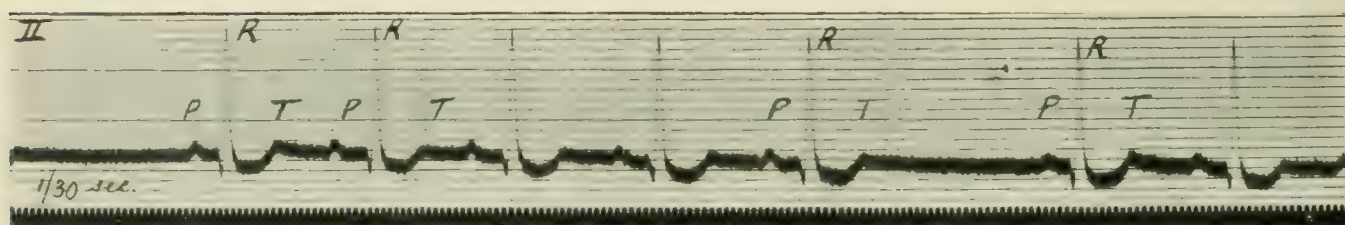


Fig. 5. Electrocardiogram of CASE 5 under digitalis (August the 24th).

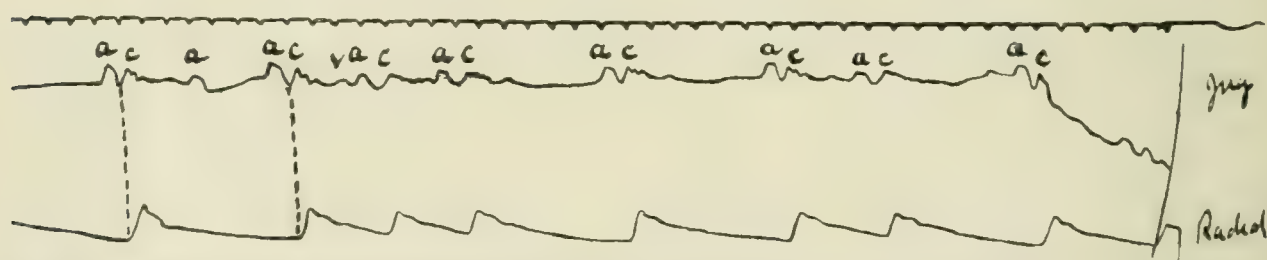


Fig. 6. Polygraph record of jugular and radial pulse of CASE 5 under digitalis (August the 25th).

*Summary.* Digitalis caused marked sinus arrhythmia with occasional auricular extrasystoles and later long pauses of the whole heart (sino-auricular block?) and less marked auriculo-ventricular block. Atropine (1/50 and 1/25 gr.) had no effect on either of these abnormalities and did not accelerate the heart appreciably, although it caused fair acceleration before the digitalis treatment had been instituted and after it had been abandoned.

### Discussion.

In the first three of these cases the injection of atropine was followed by the disappearance of the slowing and irregularity induced by digitalis and these may accordingly be ascribed to the inhibitory action. It is true that during or after digitalis treatment the heart released from inhibition did not quite attain the rate of the released heart before digitalis treatment. But the difference is not marked, and it is impossible to determine how far it is due to the digitalis and how far to the rest and general treatment. Several



writers have removed block or sinus slowing after digitalis by the use of atropine, so that the inhibitory character of these irregularities under digitalis is generally recognised.

In *CASE 4* atropine removed the sinus arrhythmia and partial heart-block when they were slight in extent but failed to modify the rhythm when the regular 2:1 rhythm was developed by the continued use of digitalis. This would suggest that the block was at one time inhibitory in character and at another time due to direct action of digitalis on the heart. But closer examination indicates that at both times there was direct action on the conduction. For on April the 5th and July the 17th the block was much diminished by atropine but was not entirely removed except for a few minutes, frequent intermissions occurring soon afterwards. There was no tendency to heart-block before digitalis was administered except in so far as the *a-c* interval was long, and when atropine was injected while the patient was not under the influence of digitalis there was no failure in the conduction of even rapid rhythm. Digitalis therefore lessened the conduction through a direct action on the heart and also through its inhibitory stimulation. The combination of these two factors caused heart-block on April the 5th and July the 17th, and atropine removed this by eliminating the inhibition, the direct action on conduction remaining unchanged but not being powerful enough to manifest itself in intermissions. In a more advanced stage of digitalis action (July the 3rd) the direct action on conduction had been so far developed that half rhythm was present quite apart from any inhibitory action. And atropine therefore failed to remove the half rhythm, though a very slight sinus arrhythmia disappeared under it.

In *CASE 5* the very marked irregularities under digitalis arose from sinus disturbance and from auriculo-ventricular block, and these were unaffected by atropine and therefore arose from direct action on the heart and not from the inhibitory activity.

In these five cases of normal rhythm, digitalis caused slowing and block, sometimes through the inhibitory apparatus and sometimes through direct action on the heart muscle which closely simulated the inhibitory stimulation in its effects. This close simulation of the inhibition is of interest because a similar apparent inhibition has long been known in the frog's heart under digitalis and in fact has only recently been shown not to be inhibitory in nature (Werschinin,<sup>19</sup> Straub<sup>16</sup>).

## II. FIBRILLATING CASES.

In those cases in which auricular fibrillation is present digitalis reduces the pulse much more frequently and the reduction is greater in degree as a general rule. Thus in Mackenzie's sixteen cases of auricular fibrillation there was marked slowing in thirteen after digitalis, squills and strophanthus. This is probably the form of disease in which digitalis obtained its reputation as a cardiac sedative, and as the slow pulse is in most cases accompanied

by marked improvement in the general symptoms the curative effect has been ascribed to the slowing. In several cases some improvement occurred in the general symptoms even when the pulse was not noticeably slower, but it is impossible to state whether this was due to the action of the drug or to the rest and general hospital treatment. At the same time it cannot be stated fairly that digitalis is without beneficial action in these cases even when the pulse is unchanged in rate.

The specific action of digitalis on the rate of the pulse in auricular fibrillation is most easily explained by supposing that it lessens the conductivity of the auriculo-ventricular bundle and thus lessens the number of impulses reaching the ventricle, which accordingly beats more slowly (Lewis<sup>8</sup>). And digitalis induces block in a certain proportion of cases of normal rhythm through its inhibitory action, so that it seemed probable that the slow pulse under digitalis in auricular fibrillation arises from inhibitory blocking of the bundle. This view is supported by a number of facts observed experimentally and clinically. Thus it has been shown by a number of experimental investigations that in auricular fibrillation in animals stimulation of the vagus slows the ventricle and makes it more regular although the fibrillation continues in the auricle. And block induced by other means such as asphyxia causes a similar reduction in the rate of the ventricle during auricular fibrillation. A strong argument in favour of this view has also been given by Wenckebach<sup>18</sup> who found that pressure on the vagus nerve in auricular fibrillation in man often causes marked slowing of the pulse in the same way as digitalis, and that in one case in which this vagus stimulation failed to affect the pulse, digitalis was equally ineffective. The chain of evidence thus seemed complete; both in animals and man stimulation of the vagus nerve slows the pulse whether the rhythm is normal or fibrillating; digitalis also reduces the pulse in animals and man, and in the normal rhythm does so mainly through vagus stimulation, as is shown by the acceleration when the inhibition is removed by atropine; further in one case of auricular fibrillation (Wenckebach) in which digitalis was ineffective, vagus stimulation also failed to reduce the pulse. It remained only to perform the crucial experiment of eliminating the inhibition during the action of digitalis in auricular fibrillation.

*CASE 6.* S.W.,\* aged 35, female, was admitted on July the 26th, 1910, complaining of shortness of breath and throbbing of the heart. There was no definite history of rheumatism. Auricular fibrillation with a rapid irregular pulse 125 per minute was diagnosed. Digitalis reduced the pulse to 66 per minute and relieved her symptoms but induced headache and nausea, and when it was stopped the pulse soon rose to over 100.

On December the 9th (Fig. 7, A) she had been off all drugs for eight days, and the pulse rate had risen to between 90 and 100 per minute. A tracing was taken, and atropine sulphate, 1/50 gr., was injected, and the pulse rate recorded by the polygraph (Fig. 7, A). It began to rise in twelve minutes after the injection, and then maintained a rate varying from 134 to 144 per minute. Dryness of the throat was complained of in eighteen minutes. Increase of rate, 44 per minute.

She was then placed on digitalis, and had taken 5 dr. by December the 16th, and this amount had produced nausea and severe headache. Pulse-rate had fallen to 60-64 per minute. The

---

\* Cited by Silberberg, *CASE 1*.



tracing was taken as before, and the same dose of atropine sulphate, 1/50 gr., given. The pulse-rate began to rise in nine minutes, and reached a rate of 76-84 per minute (Fig. 7, B). Increase, 18 per minute. Throat dry in twenty-two minutes. For Summary, see Table 1

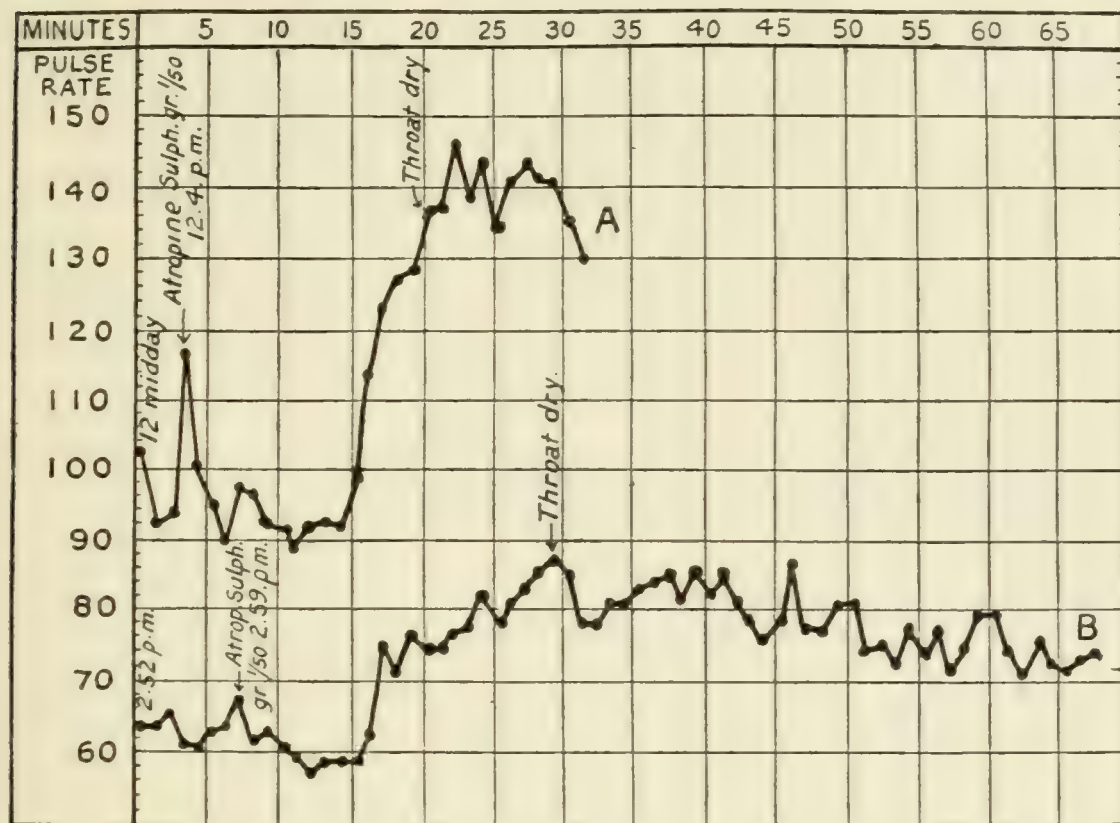


Fig. 7. (CASE 6). Chart of pulse rate under atropine. A, without digitalis. B, after digitalis (5 dr.).

**CASE 7.** H.G.,\* aged 24, male, carman, was admitted on January the 23rd, 1911, complaining of shortness of breath, palpitation, and cough. History of rheumatic fever and œdema. Diagnosis of mitral stenosis and auricular fibrillation.

On January the 31st (Fig. 8, A), atropine, 1/50 gr., was given and increased the pulse from 76-86 per minute to an average rate of 130-140, maximum 150. Increase, 53 per minute.

The pulse fell to 60 after seven days of digitalis treatment, and on February the 21st (Fig. 8, B), when 15 dr. of digitalis had been taken, atropine 1/50 gr., was given and produced a rise from 66-72 to 74-86. Increase, 11. Throat dry in 23 minutes.

On February the 24th (Fig. 8, C), after 18 dr. of digitalis, the pulse was 54-60, and atropine, 1/25 gr., increased it to 76-84. Increase 23. Throat dry in 20 minutes.

The 1/25 gr. atropine in this second observation is in the nature of a control, and as the maximum pulse-rate is no higher than with 1/50 gr., one may consider that 1/50 gr. is a sufficient quantity to fully remove vagal inhibition. For Summary, see Table 1.

**CASE 8.** C.W.,† female, aged 42, acrobatic dancer, was admitted on March the 5th, 1911, complaining of shortness of breath on exertion during the last two years. History of acute rheumatism. Mitral stenosis and auricular fibrillation. Heart-rate, 90-112, not slowing on rest in bed.

On March the 15th atropine sulphate (1/50 gr.), increased the rate from 120-130 to 180-190 per minute (apex tracing). Increase of rate, 60 per minute.

Tincture of digitalis, 20 m. t.d.s., induced nausea and reduced the pulse to 68 in seven days and had to be stopped owing to nausea. Some days later when nausea was still present atropine (1/50 gr.) increased the pulse from 70 to 90-96 per minute. Increase, 23. Throat dry in 13 minutes. Summary given in Table 1.

\* CASE 2, Silberberg.

† CASE 3, Silberberg.

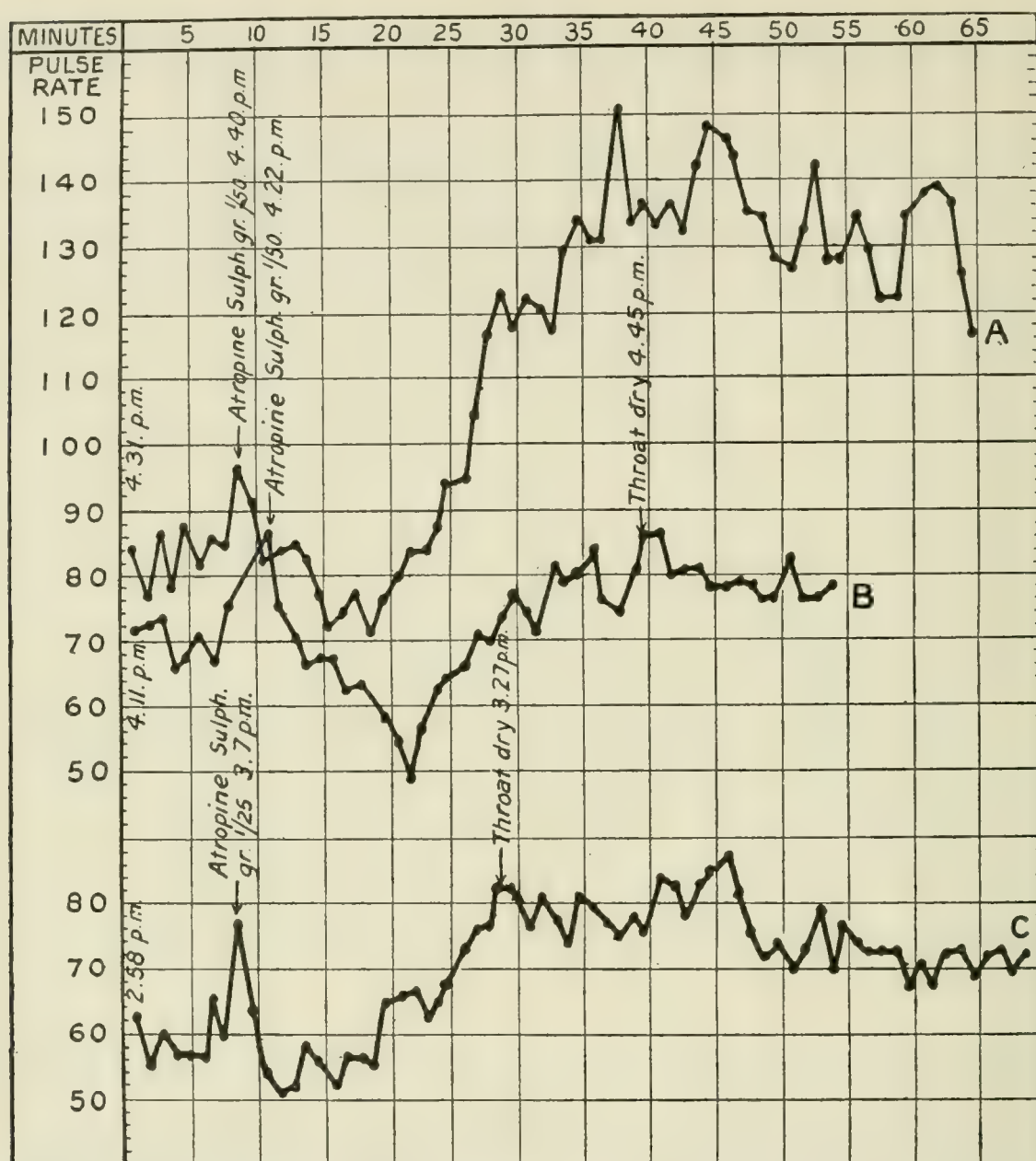


Fig. 8. (CASE 7). Chart of pulse rate under atropine. A, before digitalis. B, after 15 drs. tincture digitalis. C, after 18 drs. tincture digitalis.

**CASE 9.** D.W.,\* female, aged 17, was admitted on October the 26th, 1910. History of chorea and rheumatic fever. Mitral stenosis and auricular fibrillation, pulse 144. Some œdema of lungs and marked dyspnœa. She responded rapidly to digitalis, her pulse showing prompt and marked slowing under its influence. On several occasions it induced long periods of coupled beats, 36-40 at the wrist, 72-80 at the apex.

On December the 1st under digitalis the heart-rate was 76-78, coupled rhythm (apex tracing). Atropine sulphate, 1/50 gr., caused dryness in the throat in eleven minutes and the pulse-rate began to rise in nineteen minutes and reached 86-92 per minute, and the coupled rhythm began to break from this time onwards, so that there were phases of non-coupled beats mixed with occasional couples. The continuous coupled rhythm returned in about three hours after the injection.

The injection was repeated the following day and gave a similar result. She was allowed to come out of the influence of digitalis, and on December the 14th (twelve days later) her heart-rate varied from 110-130 per minute, irregular, with occasional coupled beats.

Atropine, 1/50 gr., increased the rate to 170-176 per minute after ten minutes, this rate beginning to pass off in an hour, and finally slowing to about 120. There was an occasional coupled beat present even at this very rapid rate. Increase in rate, 53 per minute, as opposed to 12 while under digitalis. See Table 1.

\* CASE 4, Silberberg; CASE 5, Mackenzie.



**CASE 10.** W.W.,\* male, aged 35, was admitted on February the 18th, 1910, complaining of shortness of breath and swelling of the legs. History of rheumatic fever twice and of sudden seizure with shortness of breath and tightness across the chest. Diagnosis of mitral stenosis and auricular fibrillation with dyspnoea, oedema and enlarged and pulsating liver. Pulse rapid and irregular, about 90 per minute. He always gave a prompt reaction to digitalis as regards slowing of the pulse, though it produced severe headache.

On December the 9th he had been without drugs for six full days. His pulse rate was 70-80 per minute. An injection of 1/50 gr. atropine was given hypodermically, and the pulse began to rise in twelve minutes and finally reached 90-100 per minute. Dryness of the throat came on in about twenty minutes. Increase in pulse rate, 20 per minute.

On December the 11th he was put on tincture of digitalis, at first 20 m. t.d.s., and after three days on 10 m. t.d.s. On December the 21st he complained of severe headache and had vomited; he had then taken 3 1/2 dr. Pulse rate, 58-60; atropine was injected and it began to rise in sixteen minutes, and reached 84-92, an increase of 29 per minute. (Table 1.)

**CASE 11.** A.M.,† male, aged 67. Cardio-sclerosis and auricular fibrillation.

On February the 27th, 1911, atropine, 1/25 gr., increased the pulse from 118-122 per minute to 120-132, an increase of 6 per minute.

On March the 4th he was put on tincture of digitalis, 20 m. t.d.s.; it produced nausea and was stopped on March the 13th. Atropine, 1/50 gr., now raised the pulse rate from 64-74 to 68-74; average increase, 2 per minute. (Table 1.)

**CASE 12.** W., carman, aged 45. No history of rheumatism, chorea or venereal disease. Healthy till 1905. Then dyspnoea and pain in epigastric region, especially after exertion. Since 1908 some swelling of ankles which always disappeared on rest. Lately worse, and since two weeks severe palpitation.

Marked cyanosis, no orthopnoea. Some icterus and lung oedema.

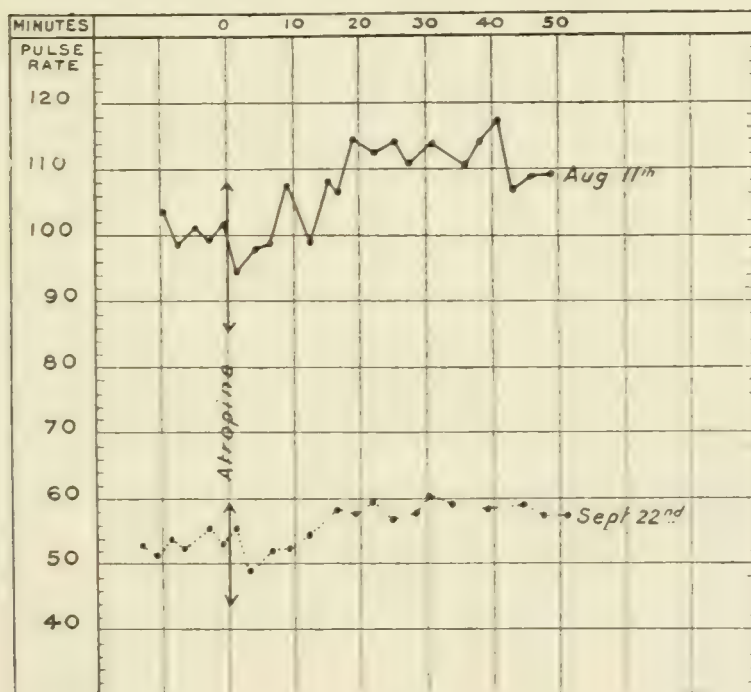


Fig 9.

Fig. 9. Chart of pulse rate (**CASE 12**). August the 11th, before digitalis,———. September the 22nd, under digitalis,.....

Heart reached third space 1 1/2 in. to right, 6 in. to left of sternum. Diastolic thrill at apex, and loud musical systolic bruit and faint diastolic at apex. Pulse 100 per minute, and polygraph showed auricular fibrillation. No precordial tenderness. Base of left lung dull and fine crepitations on both sides, especially on the left. Liver dulness 2 in. below ribs and some tenderness over it. Moderate oedema in both feet.

Admitted July the 19th. Developed carbuncle which was incised and healed. Temperature normal August the 8th. Oedema had disappeared but palpitation remained.

August the 11th, atropine 1/50 gr., raised the pulse from 100-110 to 110-115 (Fig. 9).

\* **CASE 5**, Silberberg.

† **CASE 6**, Silberberg.

August the 15th. Tincture digitalis m. 20, t.d.s. was ordered. The apex beat was then 105-109, but fell to 75 on the 21st, and to 60 on the 26th. There was no longer palpitation and considerable improvement of the other symptoms had occurred.

August the 30th. Apex 50. Some nausea and headache was complained of and these increased on September the 1st when the pulse was 50 per minute with some coupled beats. Digitalis was stopped owing to vomiting and depression.

September the 5th. Pulse 54. Headache and nausea disappeared.

September the 11th. Digitalis resumed. Pulse 76, and fell to 55 on the 14th and symptoms were much improved.

September the 20th. Pulse 55-70 (since the 15th).

September the 22nd. Pulse 52. Injection of atropine, 1/50 gr., increased pulse rate to 56-59 (Fig. 9). Pulse later remained 60-70 until October the 14th when he returned to work. (Summary given in Table 1.)

**CASE 13.** H.F.C., hatter, aged 50. Chorea at 6 years of age. No history of rheumatic fever or syphilis. In 1908 suffered from palpitation on exertion. In 1909 had pneumonia and has been under treatment for heart disease since. This led to improvement until three weeks ago when he found the dyspnoea increasing and the feet beginning to swell. Admitted, July the 17th, 1911.

The patient complained of giddiness and breathlessness, especially on exertion. There was some tenderness over the liver, some oedema of the feet, slight emphysema with fine crepitations over the base of the lungs. The heart impulse was in the fifth and sixth interspace. Dulness extended one inch to the right and  $6\frac{1}{2}$  inches to the left of the sternum. Mitral systolic murmur at apex which was transmitted to base. Polygraph tracings showed fibrillation of the auricles, and a pulse rate of 120-125, increased to 160 after climbing stairs. Urine, 41 ozs. Little improvement was observed from fourteen days rest in bed, the pulse remaining at 125-130, the urine sinking to 31 ozs., but the dyspnoea being less marked.

July the 29th. Atropine, 1/50 gr., increased the pulse from 104-112 to 148-159 per minute.

July the 31st. Digitalis tincture, m. 20 t.d.s.

August the 5th. Slight giddiness and nausea. Pulse 75 per minute, rising to 80 on climbing stairs.

August the 12th. Some nausea. Pulse 61, rising to 65 on climbing stairs. Bases of lungs clear and no oedema anywhere. Slight precordial tenderness. Digitalis stopped. An injection of atropine (1/25 gr.) caused preliminary slowing followed by a rise in the pulse to 74-84 from an original rate of 64-69. (See Table 1.)

**CASE 14.** C., Italian, aged 27, asphalter. Admitted May the 30th, 1911. Rheumatic fever, 1900 and 1902. 1904 heart disease, and has since had attacks of shortness of breath and swelling of legs in 1909, 1910 and 1911.

Considerable dyspnoea, moderate anasarca. Heart reached to third rib,  $1\frac{3}{4}$  inches to right of sternum, 9 inches to left; diffuse impulse in sixth and seventh spaces. Murmurs at apex, systolic and diastolic. Aortic base, loud systolic. Pulmonary base, second sound accentuated. Dulness did not change with posture. Rhythm, total irregularity 85 per minute. Polygraph tracing showed auricular fibrillation. Liver 3 inches below costal arch in mid-clavicular line. Some tenderness over precordium and epigastrium. Moderate oedema of both lungs. Probably under digitalis when admitted. Occasional trace of albumen in urine. Rest in bed for a week improved general condition. Oedema disappeared except from lungs. No tenderness anywhere. Pulse 83.

June the 7th. Atropine (1/50 gr.) injected, raised pulse from 87 to 130-140 (Fig. 10). Digitalis m. 20 t.d.s. was ordered and he quickly responded, the pulse falling to 76 on the 8th and to 73 on the 9th.

June the 12th. Pulse 66. Atropine (1/50 gr.) injected, and pulse rose from 68 to 102 (Fig. 10).

June the 16th. Pulse 62. Atropine (1/50 gr.) raised pulse from 65 to 80-84 (Fig. 10).

June the 19th. Pulse 60. Patient began to complain of nausea, which was worse on the 20th.

June the 21st. Depression and nausea. Pulse 53. Digitalis stopped. Atropine (1/50 gr.) raised pulse from 57 to 76 (Fig. 10).

June the 24th. Dyspnoea increased. Pain in epigastrium.

June the 26th. Atropine (1/50 gr.) raised the pulse from 74-76 to 84-86 (Table II.)

June the 27th. Symptoms more marked. Pulse 66-70.

July the 1st. Pulse 70. Dyspnoea increased and occasional palpitation.

July the 3rd. Pulse 84. Atropine (1/50 gr.) increased it to 93. (Table II.)

July the 18th. Pulse 100. Considerable palpitation.

July the 21st. Atropine (1/50 gr.) raised pulse from 96-98 to 140-145. (Table II.)

Case continued by strophanthin (intravenous).

**CASE 15.** B.H., aged 14. No history of rheumatism, scarlet fever or chorea. Illness is dated from first menstrual period three or four months before admission, since when she has had



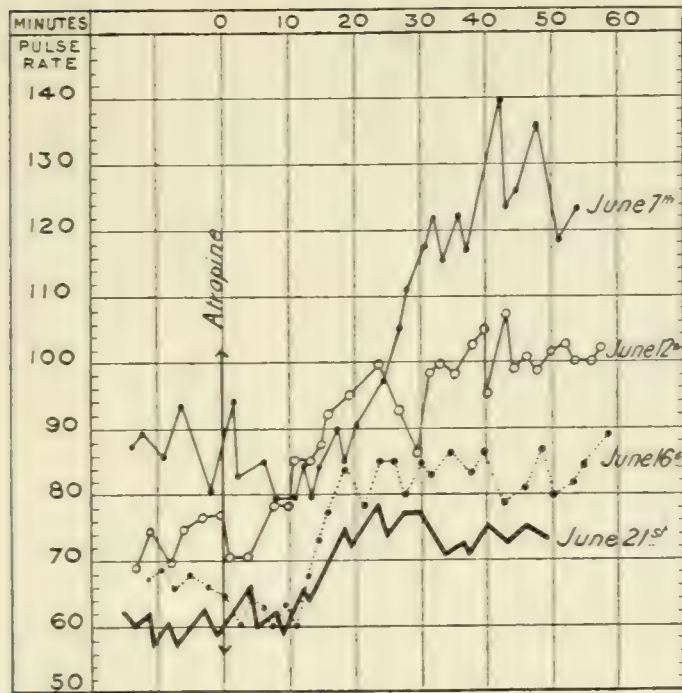


Fig 10.

Fig. 10. (CASE 14). Chart of pulse-rate under atropine.

June the 7th. ————— previous to digitalis treatment.  
 June the 12th. o—o—o after  $4\frac{1}{2}$  drs. digitalis tincture.  
 June the 16th. . . . . after 9 drs. digitalis tincture.  
 June the 21st. ————— after  $14\frac{1}{2}$  drs. digitalis tincture.

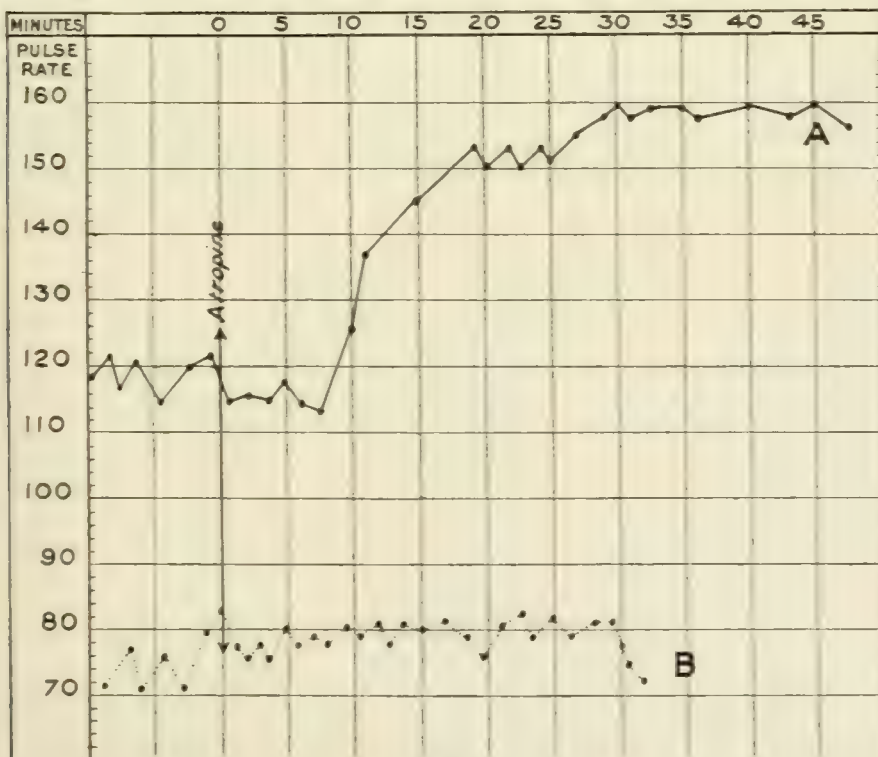


Fig 11

Fig. 11. (CASE 15). Chart of the pulse rate under atropine. A, before digitalis (September the 8th). B, under digitalis (September the 28th).

frequent vomiting. But she has always been short of breath, getting worse since May, 1911. Recently noticed swelling of feet and abdomen, and cough. She had apparently been taking digitalis before admission.

On admission (August the 28th) some cyanosis and dyspnoea. Heart  $1\frac{1}{4}$  inches to right and 6 inches to left of middle line, extending to third rib. Apex beat in sixth space. Pulse rate about 88, fairly regular, but the polygraph showed auricular fibrillation to be present. Shifting dulness in flanks, oedema of legs and face. Liver extends 2 inches below the costal arch and there is tenderness over it. Urine averaged 17 oz. with some albumen. Weight on admission 7 stone  $8\frac{1}{2}$  lbs., and had now risen to 7 stone  $10\frac{1}{2}$  lbs., and there was increased ascites and oedema of the forearms. Rest in bed until September the 8th. Heart-rate had quickened to 115-120 per minute. Urine very scanty, 5-10 oz. Atropine (1/50 gr.) injected hypodermically increased the pulse from 120 to 160 per minute in 30 minutes (Fig. 11). Ordered tincture digitalis m. 20 t.d.s.

September the 11th. She had improved rapidly.

September the 12th. Headache and depression. Apex shows almost complete bigeminus of 70-80 per minute. The radial pulse was about 45, only about half the heart beats being transmitted. Digitalis reduced to m. 10 t.d.s.

September the 14th. Apex 70. The urine had increased up to an average of 45 oz. and the weight had fallen to 5 stone  $11\frac{1}{2}$  lbs.

September the 15th. Digitalis, m. 15 t.d.s.

September the 18th. Dyspnoea and oedema gone. Apex beat 65. Still bigeminus. Felt well.

September the 21st. Allowed to get up out of bed.

September the 22nd. Digitalis, m. 20 t.d.s.

September the 26th. Improvement continued. Apex beat, 80. Radial 40, very powerful pulsations. Complete bigeminus (Fig. 12). Liver scarcely palpable.

September the 27th. Frontal headache and vomiting. Apex beat 75. Digitalis stopped. Urine decreased to average of 11 oz. per day.

September the 28th. Atropine (1/50 gr.) raised the pulse from 71-79 to 74-81. Bigeminus pulse remained unchanged. (Fig. 11).

October the 3rd. Has now no nausea or headache. Apex beat 85. The case was treated later by strophanthin intravenously.

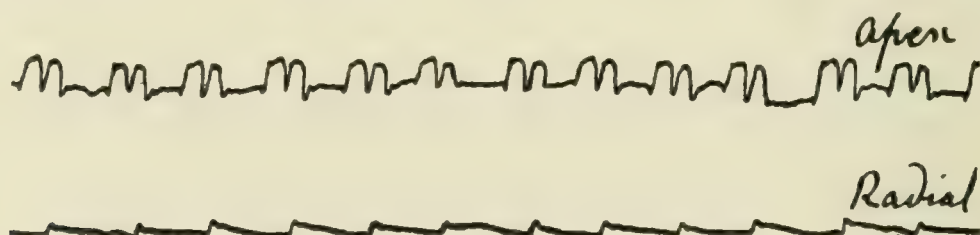


Fig. 12. Apex and radial pulse in CASE 15, showing bigeminus apex.

### Summary and discussion.

TABLE I.

| Case. | Rate without digitalis. | Rate of released* heart without digitalis. | Rate under digitalis | Rate of released* heart under digitalis. |
|-------|-------------------------|--|----------------------|--|
| 6     | 90-100                  | 134-144                                    | 60-64                | 76-84                                    |
| 7 { a | 76-86                   | 130-140                                    | 66-72                | 74-86                                    |
| b     | —                       | —  | 54-60                | 76-84                                    |
| 8     | 120-130                 | 180-190                                    | 70                   | 90-96                                    |
| 9     | 110-130                 | 170-176                                    | 76-78                | 86-92                                    |
| 10    | 70-80                   | 90-100                                     | 58-60                | 84-92                                    |
| 11    | 118-122                 | 120-132                                    | 64-74                | 68-74                                    |
| 12    | 106-110                 | 124  | 52                   | 55-59                                    |
| 13    | 104-112                 | 148-159                                    | 64-69                | 74-84                                    |
| 14    | 83-87                   | 130-140                                    | 57                   | 76                                       |
| 15    | 120                     | 160  | 71-79                | 74-81                                    |

\* i.e., Heart released from inhibitory control by the injection of atropine.



In all these ten cases of auricular fibrillation digitalis caused very distinct slowing of the pulse along with general improvement in the symptoms, but the auricular fibrillation continued unchanged. Atropine accelerated the pulse greatly before the digitalis treatment except in *CASE* 11, *i.e.*, the heart was held in check in all (except No. 11) by a well developed tone of the inhibitory mechanism. If the slowing of the pulse under digitalis had been due to an exaggeration of this tone, we should have expected the heart released by atropine from control to attain the same rate under digitalis as before treatment : in other words the numbers in columns 2 and 4 of the table should have been approximately equal in each case. The results indicate clearly that the slowness of the heart under digitalis in these cases of auricular fibrillation does not arise from an excitation of the inhibitory mechanism, but from some action on the heart itself.

The rate of the heart is under inhibitory control in these cases both before and during the digitalis treatment, for atropine accelerates it ; it may be inferred that the inhibitory mechanism is intact in these hearts and is not disorganised by digitalis. But if the amount of control exercised by the inhibitory centre may be measured by the acceleration which follows its elimination by atropine, it is found that the slow heart under digitalis is actually in a less state of repression than before it in all these cases except in *CASES* 10 and 11, in which the acceleration is comparatively slight before treatment. The same result is reached if instead of the actual number of beats the percentage augmentation is taken. The curious result is reached therefore that the slow pulse of digitalis in auricular fibrillation is not only not due to an increase in the control exercised by the inhibition (or inhibitory stimulation) but is actually accompanied by a decreased activity of that mechanism in many cases. This change in the activity of the inhibition accompanying the change in the rate of the pulse was followed more closely in *CASE* 14 (see Table 2).

TABLE II. (*CASE* 14.)

| —                | Rate of pulse<br>without atropine. | Rate of pulse<br>after atropine. | Amount of<br>acceleration. | Percentage<br>acceleration. |
|------------------|------------------------------------|----------------------------------|----------------------------|-----------------------------|
| Before digitalis | 83-87                              | 130-140                          | 50                         | 59                          |
| 6 days digitalis | 68                                 | 102                              | 34                         | 50                          |
| 10 .. ..         | 65                                 | 82-84                            | 18                         | 28                          |
| 15 .. ..         | 57                                 | 76                               | 19                         | 33                          |
| 5 .. without     | 74-76                              | 84-86                            | 10                         | 13                          |
| 12 .. ..         | 84                                 | 93                               | 9                          | 11                          |
| 30 .. ..         | 96-98                              | 140-145                          | 46                         | 47                          |

Here the control exercised by the inhibitory mechanism (columns 3 and 4) is seen to fall with the decreasing rate of the heart by digitalis and to rise roughly with the increasing rate of the heart when digitalis is abandoned. The amount of acceleration under atropine in this case gave an indication of the improvement under digitalis, the acceleration lessening with the

improvement and increasing as the patient relapsed. The same point was noted in other patients, so that it seemed possible to use atropine as a gauge of the efficacy of the treatment.

These cases show that when the digitalis action has been developed in auricular fibrillation the slowness of the ventricle and pulse is not due to stimulation of the inhibitory mechanism.

*Strophanthin in auricular fibrillation.* How little the inhibitory action is involved in the slowing of the heart in auricular fibrillation was further demonstrated in some observations on the intravenous injection of strophanthin. For this purpose we injected 1/250-1/100 gr. of strophanthin into the median vein in the usual way, the actual injection occupying about two minutes in each case. The radial pulse or the apex beat was registered continuously by the polygraph for 20-30 minutes before the injection and for 4 to 6 hours afterwards. The improvement in the condition of the patient and the reduction of the pulse from these injections was very rapid, as much progress occurring in 4-8 hours after an injection of strophanthin as in 3-4 days treatment with digitalis or strophanthus by the mouth. In a number of these observations 1/50 gr. of atropine was injected subcutaneously before or immediately after the intravenous injection of strophanthin without materially altering the progress of the case.

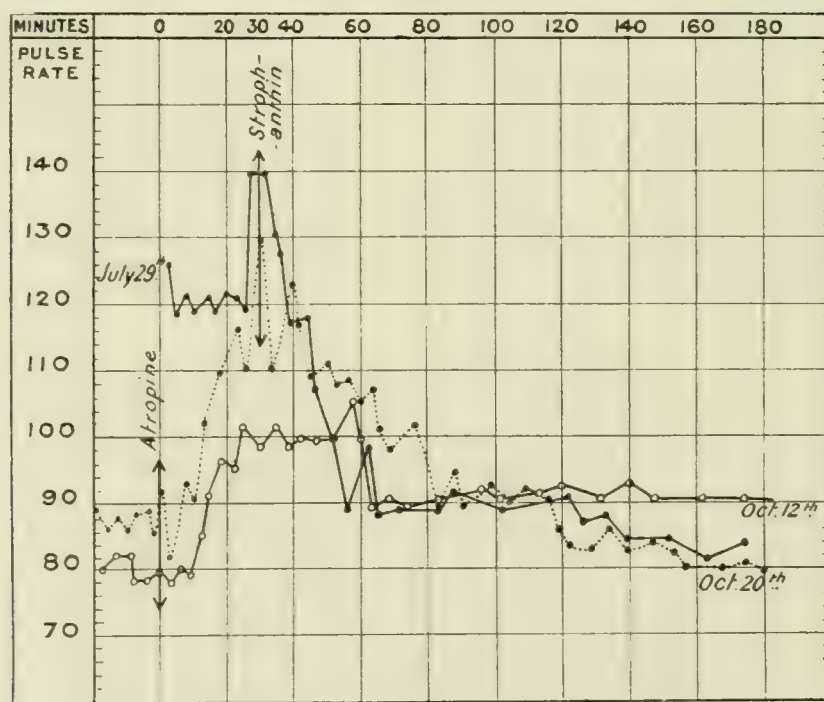


Fig 13.

Fig. 13. (CASE 14). Chart of pulse rate on July the 29th, strophanthin alone———. On October the 12th atropine alone, o—o—o. On October the 20th atropine and strophanthin ———. Atropine was injected on October the 12th and 20th at the point marked 0 on the abscissa. Strophanthin on July the 29th and October the 20th at the point marked 30.

*CASE 14, continued.*

July the 29th. Pulse for three days had been 120-125. An intravenous injection of 1/250 gr. strophanthin was made in the course of two minutes (Fig. 13), the pulse at the time being



quicken to 140 from excitement. In 10 minutes the pulse fell to 117 and continued to fall rapidly at first and then more slowly, reaching 94 in 30 minutes, 90 in 60 minutes, 89 in 2 hours, 85 in 3 hours, 80 in 4 hours, at which it remained up to 6 hours. July the 30th, pulse 84. July the 31st, pulse 88. August the 1st, pulse 94.

It then rose again gradually till after 14 days it was 100-110. *Strophanthus* tincture was given by the mouth on August the 16th, but caused vomiting and was stopped on the 18th when the pulse was about 55.

September the 5th. Pulse 110. Atropine (1/50 gr.) accelerated it to 200. After this had lasted 7 minutes 1/250 gr. *strophanthin* was given intravenously. Ten minutes later the pulse was 178, and in 30 minutes 166. In an hour after the injection of *strophanthin* the pulse was 140, in 2 hours, 135, in 3 hours, 120. Seven hours after the *strophanthin* injection the pulse was 80 and remained at this rate for six days.

Tincture *digitalis* was given from September the 12th to 21st, and the pulse remained 84-90 throughout, but rose to 100 again soon after the *digitalis* was omitted.

October the 12th, 12.24 p.m., atropine (1/50 gr.) (Fig. 13) raised the pulse from 80 to 102 by 12.50, and it remained over 100 till 1.24. The rate then fell to 90 (2.30). 3 p.m., 89; 4 p.m., 88; 5 p.m., 80.

October the 20th. Pulse 88 (Fig. 13). Atropine (1/50 gr.) injected at 1 p.m. 1.30, pulse 122-130, 1/250 gr. *strophanthin* injected intravenously. 2 p.m., pulse 100; 2.30 p.m., pulse 90; 3 p.m., pulse 88; 3.30 p.m., pulse 79; 4 p.m., pulse 79; 5 p.m., pulse 79, 1/50 gr. atropine; 5.13 p.m., pulse 93; 5.50 p.m., pulse 93.

In this case the previous injection of atropine did not prevent the subsequent intravenous injection of *strophanthin* from slowing the pulse.

*CASE 16.* S.R., female, aged 35. She had been treated previously in the hospital in 1910 for heart disease. The rhythm was then normal and *digitalis* had no apparent effect on the heart and blood pressure. (See Mackenzie, *CASE 20*). She kept fairly well after her discharge from the hospital on May the 23rd until October, 1911, when she began to suffer from cough and increasing dyspnoea. The precordial pain had returned and also swelling of the feet. Admitted January the 3rd, 1912.

Desperately ill. Orthopnoea. Deeply cyanosed. Icteric colour. Considerable ascites, Heart-rate 140-150, irregular. Auricular fibrillation. Lungs, fine crepitation everywhere. Liver enlarged. Urine scanty, 8 oz., with some albumen. She could hold her breath only four seconds. Rest in bed was ordered, and improved the symptoms, the heart rate falling to 90, and the urine rising to 25 oz. and then gradually decreasing.

January the 18th. Sudden relapse. Liver large and tender. Heart-rate, 130-145. Constant cough. Brandy 1½ oz. and 1/6 gr. morphin.

January the 19th (Fig. 14). Vomiting. Liver extremely tender, below umbilicus. No ascites. Lungs: bases dull, and râles and crepitations general.

At 2.20 p.m. Heart, 140-150. No defined apex beat. Record of polygraph taken from epigastrium.

3 p.m. 1/100 gr. *strophanthin* injected intravenously in 12 minutes.

3.17 p.m. Heart 110 per minute. The epigastric pulsation disappeared about 3.20, and the apex impulse was now well marked and used for polygraph.

3.30 p.m. Heart 80 per minute and bigeminus.

4.6 p.m. Heart 74. Patient very greatly improved, vomiting ceased. Dyspnoea, which was very marked before injection, relieved. Slept well. Heart remained about 80-90 next morning. Cough better. Nausea disappeared.

January the 21st. Heart 92. Liver had receded and was now only half an inch lower than costal margin. No tenderness over liver but slight tenderness over precordium. Less icterus.

January the 26th. Had remained fairly well since the 20th, but heart rate now began to rise, reaching 116. Respiration, 30 per minute.

January the 29th. 1/250 gr. *strophanthin* injected intravenously again reduced pulse to 75.

January the 30th. General condition improved. Pulse 84.

January the 31st. Pulse 110 or more.

February the 1st. Condition very much the same as on January 19th. Vomiting, great tenderness over liver and extensive pulsation in epigastrium from which a polygraph tracing was obtained.

7.10-7.30. (Fig. 14). Rate 150 per minute on the average.

7.30 1/250 gr. *strophanthin* injected intravenously in two minutes. Immediately followed by 1/50 gr. atropine hypodermically.

7.50. Heart 110 per minute. Epigastric pulsation had disappeared, the apex beat becoming distinct.

8.00. Pupils widely dilated, and she complained of thirst and dryness of throat.

8.30. Pulse still 110.

February the 2nd. Pulse 94, and general improvement as on previous occasion.

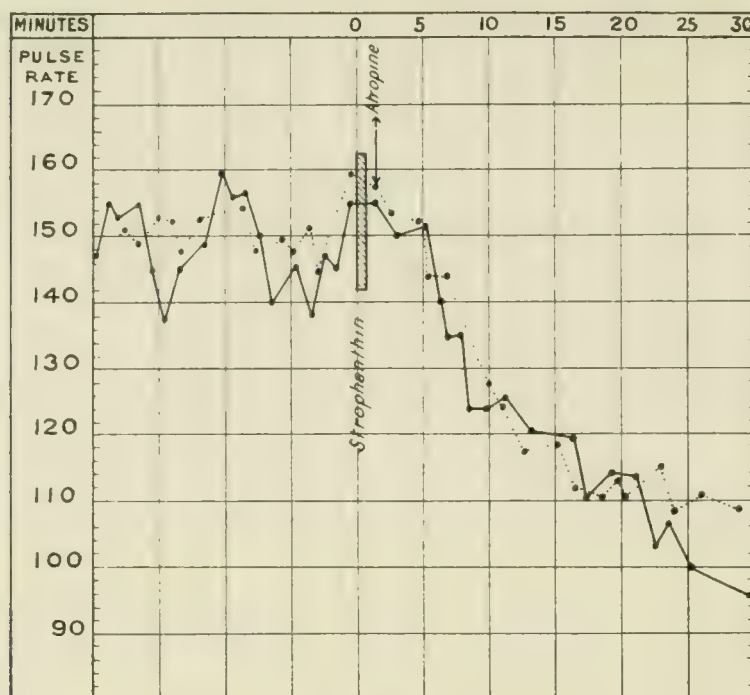


Fig 14

Fig. 14. Chart of pulse rate (CASE 16). January the 19th, ——— strophanthin alone. February the 1st. ..... Strophanthin and atropine.

In this case the chart (Fig. 14) shows the fall in the heart rate to be the same in character whether atropine was given or not. The pulse was not reduced to quite the same extent on the day on which atropine was injected but the dose of strophanthin was only two-fifths of that previously used.

#### CASE 15, continued.

October the 10th. Increasing dyspnœa, but felt moderately well with gradually accelerating pulse rate.

October the 24th. Pulse of 128 for 30 minutes and then rose to 155 from excitement.

1.25. Strophanthin (1/250 gr.) intravenously injected (Fig. 15).

1.35. Pulse 115 and remained at 105-110 until 2.30, then began to rise and had reached 125 at 3.00. When preparations for another injection were made it rose to 155 and was beating at this rate when the second injection was given.

3.30, pulse 125; 4.30, pulse 110; 5.00, pulse 113.

October the 25th. Pulse 90.

October the 31st. Pulse had now risen to 120. Tincture strophanthus m. 20 t.d.s. was ordered and reduced the rate to 100 in two days, and to 50 (apex) in three days with some bigeminus. Nausea and vomiting began and strophanthus was stopped, only 3 drs. having been given altogether.

November the 12th. Felt fairly well but dyspnœa increasing.

November the 13th. Dyspnœa much increased and pulse 130-135. Urine averaged 15 oz.

2.45. Injection of atropine (1/50 gr.) caused preliminary slowing of pulse and then accelerated it to 170 after 3.20. (Fig. 15).

3.30. 1/250 gr. strophanthus injected intravenously and after 3.40 the pulse had fallen to 143 and severe headache was complained of. During the next hour it fell to 135 (4.40). A more rapid fall then occurred so that at 5.15 the pulse was 110, and at 7.00 105.

November the 14th. Pulse 108-110.

In this case (Fig. 15) the fall induced by strophanthin was similar in character whether atropine had been injected or not, but its extent was very much smaller after atropine. This is not due to the two drugs



antagonising each other, but arises from the fact that the normal inhibition was in play throughout the strophanthin action in the one case, whereas it was eliminated when atropine had been injected previously.

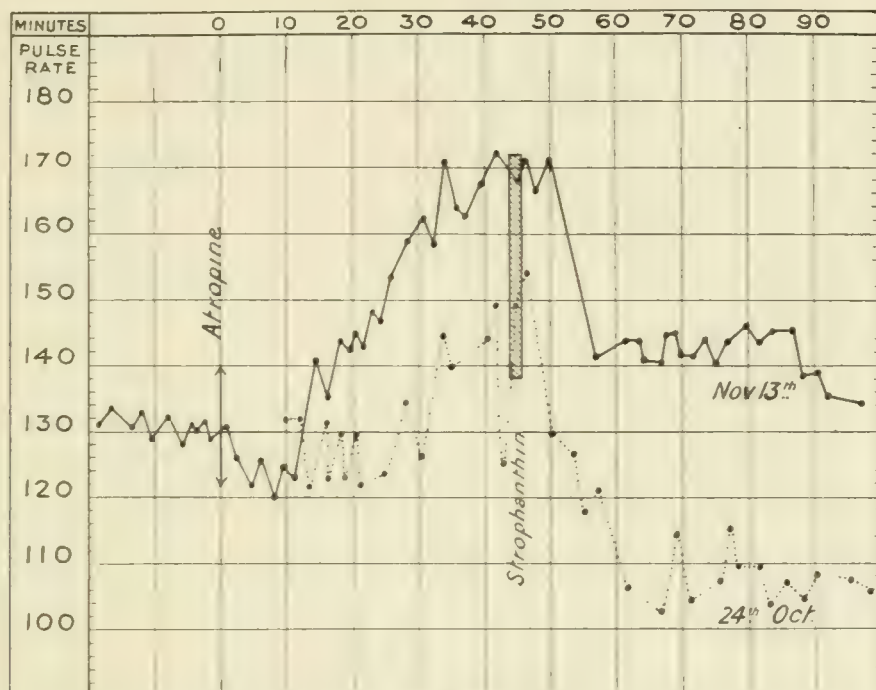


Fig 15.

Fig. 15. Chart of heart-rate under strophanthin alone (—) on October the 24th, and under strophanthin and atropine November the 13th (—).

### *Summary of strophanthin cases.*

In these three instances the reduction in the rate of the pulse and the improvement in the general condition were not prevented by the elimination of the inhibitory mechanism by atropine. It is true that in some instances the pulse was not so slow two or three hours after the combined action of strophanthin and atropine as at the corresponding period after strophanthin alone, but this is due to the fact that in the latter case the ordinary degree of inhibition was present, while under atropine this was eliminated. The curve of the fall in pulse rate was the same after strophanthin whether atropine was injected or not, and strophanthin slows the heart even when the inhibition is put out of action.

### GENERAL RESULTS.

These observations show finally that the inhibition is not involved in the therapeutic effects of digitalis and in fact in non-fibrillating cases the stimulation of the inhibitory centre by the drugs of this series is a distinct drawback to their use owing to its serving to induce block. The reduction

in the rate of the pulse under digitalis is largely, though not exclusively, inhibitory in origin in the non-fibrillating cases, but in cases of auricular fibrillation increased inhibition seems to play no part in the slowing of the pulse.

The cause of the slow digitalis pulse in auricular fibrillation must thus be sought for in some other action than in the stimulation of the inhibition, and the natural suggestion is that the multitudinous stimuli descending from the auricle are prevented from reaching the ventricle by a block arising from the direct action of digitalis on His' bundle. Mackenzie at one time supposed that block was caused by digitalis in normal rhythm only when there was a previous affection of the bundle which might be measured in unusual prolongation of the *a-c* interval, but this has not proved to be present uniformly. And Lewis suggested that only those cases of auricular fibrillation showed reduction of the pulse in which there was previously some insufficiency in the conducting power of the bundle. This seems improbable, however, for digitalis slows the pulse especially in those cases in which the previous rhythm is very high and in which the conduction may therefore be supposed to be fairly competent, while in other cases in which the pulse is only 60-70, and in which the conduction would appear to be less perfect, the rate is less affected by digitalis.

Apart from this question however, the slowing of the pulse in auricular fibrillation may be explained most easily by a partial block of the auriculo-ventricular bundle, and it is therefore necessary to consider what evidence there is that block may be induced by the direct cardiac action of digitalis as apart from its effects on the inhibitory mechanism. In the frog auriculo-ventricular block may be observed not infrequently if the minimal fatal dose be injected; and this block is independent of the inhibitory mechanism for it occurs after atropinisation. In mammals the ordinary block developed under digitalis is inhibitory, but one of us<sup>1</sup> has described a condition arising from large doses of digitalis in atropinised hearts, in which impulses fail to pass the bundle of His in either direction. This suggested a re-examination of the action of smaller quantities of these bodies on the conduction, and several experiments were performed on anæsthetised and atropinised dogs, in which the exact *As-Vs* interval was measured under the intravenous injection of 0.5 mg. strophanthin.

The figures obtained from one such experiment may be given to show the uniformity of the rate of conduction from auricle to ventricle under a dose of strophanthin which injected in the same way in cases of auricular fibrillation in man is sufficient to reduce the heart rate very considerably in half an hour.

December the 4th, 1911. A dog was anæsthetised with morphine, paraldehyde and a few drops of chloroform, the vagi were cut and the myocardiograph applied to the right auricle and right ventricle. Time was measured in 0.01 secs.,



| TIME. | RATE<br>PER MIN.   | A-V INTERVAL. | VENTRICULAR<br>CONTRACTION. |
|-------|--|---------------|-----------------------------|
| 4:00  | 200  | 0.09 sec.     | 27 mm.                      |
| 4:10  | 200  | 0.095 "       | 28 "                        |
| 4:13  | 0.5 mg. (1/130 gr.) strophanthin injected intravenously.         |               |                             |
| 4:16  | 188  | 0.095 sec.    | 33 mm.                      |
| 4:20  | 188  | 0.090 "       | 35 "                        |
| 4:30  | 188  | 0.087 "       | 34.5 "                      |
| 4:40  | 188  | 0.09 "        | 33.0 "                      |
| 4:50  | 194  | 0.085 "       | 32.5 "                      |
| 4:51  | 0.5 mg. strophanthin injected intravenously.                     |               |                             |
| 4:54  | 188  | 0.090 sec.    | 33 mm.                      |
| 4:58  | The ventricle took up its own rhythm independent of the auricle. |               |                             |

In this experiment strophanthin did not change the A-V interval in the course of 40 minutes after its injection. Measurements were taken every two minutes but it is unnecessary to give further figures as they all fell within the limits given in the table. The rate was also little changed by strophanthin while the strength of contraction of the ventricle was notably increased, and that of the auricle showed even greater augmentation.

There is thus no evidence that in the dog members of the digitalis series in ordinary quantities retard the conduction by direct action on the muscle in the way which is recognised in the frog.

In man with normal rhythm the digitalis block is generally inhibitory in origin and our CASES 4 and 5 are so far as we know the first in which the block has been proved to be independent of the inhibitory mechanism. And in fact there is no evidence except in these two cases and in observations on the frog that bodies of the digitalis group reduce conduction by direct action on the muscle. This seems an insufficient basis on which to found an explanation of the slowing of the ventricle in auricular fibrillation in man, unless other possible views be excluded.

Another explanation of the slowing in clinical cases of auricular fibrillation might be based on the digitalis substances reducing the excitability of the ventricle, for which some evidence is available. If this occurs in man, some of the weaker impulses descending from the auricle in fibrillation may fail to induce contraction and the rate of the ventricle may thus be reduced. Straub<sup>15</sup> was the first to observe that toxic doses of antiarin, which resembles digitalis in its action on the frog's heart, renders the frog's ventricle less excitable by electrical shocks and Brandenburg<sup>2</sup> confirmed this for "therapeutic" doses of digitalin also in the frog. Pletnew,<sup>12</sup> however, found that the doses used by Brandenburg were almost uniformly lethal for frogs. In the rabbit Pletnew found that digitalinum purum increases the excitability of the ventricle along with the contractility and that when large quantities are injected both functions also sink together. The excitability is only reduced in fact when the stage of irregularity is reached. Hering<sup>11</sup> mentions an experiment on a perfused cat's heart, in which after repeated injections of digitalin the electrical excitability sank until no response could be elicited even when the coil was pushed completely home. In order to determine how far this action on the excitability of the ventricle is exerted in mammals, the following experiment was performed.

*Experiment II.* A dog anæsthetised as in Experiment I. and the myocardiograph attached to the right auricle and ventricle. Vagi divided. Electrodes were hooked into the right ventricle and connected with a secondary coil. The primary circuit was broken and made by a rotating interruptor driven by a small motor at a constant rate. The minimal shock which was sufficient to induce a ventricular rhythm independent of the auricle was ascertained at intervals throughout the experiment, and is given in the following table in terms of mm. distance between the coils.

| TIME. | MINIMAL<br>EFFICIENT<br>SHOCK IN MM.         | RATE OF<br>HEART. | VENTRICULAR<br>CONTRACTIONS. |
|-------|--|-------------------|------------------------------|
| 11.53 | 79-80  | 156               | 21-22 mm.                    |
| 12.02 | 80-81  | 156               | 22-23                        |
| 12.10 | 81-82  | 156               | 27.5                         |
| 12.15 | 81-82  | 156               | 29.0                         |
| 12.16 | 0.5 mg. strophanthin injected intravenously. |                   |                              |
| 12.19 | 78-79  | 162               | 38                           |
| 12.20 | 77-78  | 156               | 40                           |
| 12.26 | 78   | 150               | 38.5                         |
| 12.40 | 79-80  | 144               | 33                           |
| 12.45 | 79-80  | 144               | 33                           |

In this experiment a slight but definite decline in the excitability of the ventricle is seen to occur after the injection of strophanthin and this decline runs parallel with the characteristic increase in the strength of the ventricular contractions, reaches its maximum at the same time and tends to disappear with the return of the contractility to the normal.

Thus in the frog in large doses and in the mammal in small amounts digitalis bodies tend to lessen the excitability of the ventricle. Whether this effect also occurs in man we have at present no means of knowing, a fall in the excitability of the ventricle cannot be distinguished from a fall in the conduction.

The slowing of the pulse in auricular fibrillation may possibly be due to a reduction of the conduction through a direct action on the bundle or to a lessening of the excitability of the receptive fibres of the ventricle through direct action on them. But while this is a possible explanation of the slowing it is not strongly supported by these experiments on animals and it is not the only available view. For it is not possible to exclude the view that the change in one or other of these functions may follow from the improved nutrition of the heart arising from the increased strength of the contractions and consequent improved circulation through the coronary system; and this action on contractility is much more definitely established by experimentation on animals than the effects on conduction and excitability, and has not been proved in man hitherto merely because we are still unable to measure the strength of the heart beat. If this view is correct one must argue that the failure of the contractility and consequent malnutrition in these cases increases the excitability or facilitates the conduction in the heart muscle and thus gives rise to the great acceleration of the heart; and the slower rate under digitalis is not the cause but the consequence of the improvement in the circulation, which follows the increase in the force and extent of the contraction. This involves the assumption that insufficient contraction and malnutrition of the heart increases the excitability or



conduction, for which there is at present no satisfactory evidence. But it seems at least as plausible as to suppose that in some of these fibrillation cases the conduction or excitability increases spontaneously and thus gives rise to the crisis in which digitalis proves so efficacious.

For example in *CASE 15* the patient was admitted with a pulse rate of 140-150 which fell to 90 on rest in bed but rose again to 130-145 a week later, the acceleration being accompanied in each case by aggravation, the slowing by amelioration, of the general symptoms. It is difficult to suppose that rest in bed could directly lessen the conduction or excitability so much as to change the rate from 140 to 90 per minute and it seems more plausible to suppose that it operated indirectly by improving the nutrition of the heart and thus reducing the activity of these functions. But if the rest in bed only affects the conduction and excitability indirectly through its immediate action on the nutrition, it is quite possible that the injection of strophanthin which had similar effects on the rate a few days later also acted indirectly on these functions by increasing the power of the contraction and thus increasing the circulation in the coronary vessels.

A remarkable feature in these very rapid hearts of auricular fibrillation is the high tonic activity of the inhibitory centre. This can be estimated by the acceleration which follows its elimination by atropine. In six of our nine observations the rate rose over 40 per cent. under atropine before the digitalis treatment, although it was much above the normal from the beginning. The intrinsic mechanism of the heart was therefore maintaining a rapid rhythm, but was opposed by the medullary inhibitory apparatus the activity of which was approximately the normal, for Müller<sup>10</sup> found the rate of the normal heart accelerated by atropine in about the same ratio as in our observations. This would suggest that the intracranial circulation was not insufficient, for when the inhibitory centre suffers from anæmia, as in hæmorrhage or under the nitrites, it loses its tonic activity and permits the heart to accelerate.

As regards the characters of the pulse tracing in our cases, the changes induced by digitalis have been sufficiently detailed by others. After atropine the pulse is quickened, but its general character is unchanged; thus before digitalis treatment is instituted atropine increases the number of small beats, but does not prevent pauses of some length and does not render the tracing more regular. When the digitalis treatment rendered the pulse more regular, atropine again quickens it, but again does not alter its character, the pulse maintaining its improved regularity throughout.

#### SUMMARY.

1. The members of the digitalis group slow the pulse in a certain number of cases in which the rhythm is given by the normal pacemaker, and as a general rule this slowing may be removed by atropine and is therefore inhibitory. In other cases, however, the sinus slowing and block are unchanged by atropine and then arise from the direct action of digitalis on the

conducting fibres from the pacemaker to the auricle and from the auricle to the ventricle.

2. In auricular fibrillation, digitalis and its allies slow the heart from some direct action on the heart and not from stimulation of the inhibitory mechanism, for atropine does not restore the original rate of the released heart. The reduction in rate may be due to a direct depression of the conduction or of the excitability of the heart muscle by digitalis. But it is suggested that these functions are reduced indirectly through the improved nutrition of the heart from the augmented power of contraction of the heart muscle. The previous injection of atropine does not materially affect the rapid reaction of the heart to the intravenous injection of strophanthin.

3. The inhibitory stimulation induced by digitalis therefore does not play any part in the beneficial action of the drug, which is to be ascribed to its direct action on the cardiac muscle solely.

#### BIBLIOGRAPHY

- <sup>1</sup> BEDDOES. "Observations on the medical and domestic management of the consumptive; on the powers and agency of digitalis; &c." London, 1801.
- <sup>2</sup> BRANDENBURG. *Zeitschr. f. klin. Med.*, 1904, LIII, 255.
- <sup>3</sup> CUSHNY. *Journ. of exper. Med.*, 1897, II, 233.
- <sup>4</sup> CUSHNY. *Journ. of Physiol.*, 1899-1900, XXV, 49.
- <sup>5</sup> FERRIAR. "An essay on the medical properties of the *Digitalis purpurea* or Foxglove," London and Manchester, 1799.
- <sup>6</sup> HERING. *Archiv. f. d. ges. Physiol.*, 1907, CXVI, 149.
- <sup>7</sup> KINGLAKE. "Cases and observations on the medical efficacy of *Digitalis purpurea* in phthisis pulmonalis." London, 1801.
- <sup>8</sup> LEWIS. *Brit. med. Journ.*, 1910, II, 1670.
- <sup>9</sup> MACKENZIE. *Brit. med. Journ.*, 1905, I, 519-522. *Heart*, 1911, II, 273.
- <sup>10</sup> MULLER (E.) "Ueber die Wirkung des atropins a. d. gesunde und kranke menschlich. Herz." Inaug. Dissert., Dorpat, 1891.
- <sup>11</sup> PEREIRA. "Elements of Materia Medica," 1840, II, 844.
- <sup>12</sup> PLETNEW. *Zeitschr. f. exper. Pathol. u. Therap.*, 1905, I, 80.
- <sup>13</sup> PRICE. *Proc. of Royal Society of Med. Therapeutic Section.* 1911, IV, 151
- <sup>14</sup> SCHMIEDEBERG. "Festgabe an C. Ludwig," 1874.
- <sup>15</sup> STRAUB. *Archiv f. exper. Pathol. u. Pharmak.*, 1901, XLV, 346.
- <sup>16</sup> STRAUB. *Biochem. Zeitschr.*, 1910, XXVIII, 392.
- <sup>17</sup> TRAUBE. "Gesammelte Beiträge zur Pathologie u. Physiologie," 1871, I, 252.
- <sup>18</sup> WENCKEBACH. *Brit. med. Journ.*, 1910, LI, 1600.
- <sup>19</sup> WERSCHININ. *Archiv. f. exper. Pathol. u. Pharmak.*, 1909, IX, 328; 1912, LXIII, 386.
- <sup>20</sup> WITHERING. "An account of the Foxglove," Birmingham and London, 1785.



## CARDIAC IRREGULARITIES IN MORPHINE POISONING IN THE DOG.

BY J. A. E. EYSTER AND W. J. MEEK.

*(From the Physiological Laboratory of the University of Wisconsin).*

THE action of morphine on the heart has been recently investigated by V. Egmond.<sup>2</sup> The heart is slowed by amounts as small as 0.04 mg. per kilo.. At first there may be an increased heart rate, lasting from five to ten minutes following the administration, and resulting from the nausea and not from any direct action on the heart. In dogs, the slowing is due exclusively to stimulation of the vagus centre. Irregularities, removed at once by vagotomy or by atropine, are not infrequent. In cats, the cardiac action is much less constant, sometimes the heart is slowed, at other times accelerated. An increased contraction in the isolated cat's heart was observed on perfusion with 0.016 per cent. morphine. After the administration of successive doses of morphine the tolerance established by certain tissues is not shared in by the vagus mechanism, which still retains its usual sensitiveness to the action of the drug. The literature is fully reviewed in this paper.

Our interest in the action of morphine on the heart was aroused by noting the occurrence of a peculiar type of cardiac irregularity in dogs after the administration of morphine and previous to general anæsthesia in animals used for various work in the laboratory. It is present in nearly all dogs an hour or more after the subcutaneous injection of 30-60 mgs. of morphine. It frequently disappears under general anæsthesia and particularly after extensive operative procedure such as that of exposing the heart for the purpose of obtaining records of the contractions of the auricles and ventricles. The electrocardiograph offered the best means for study of the cause of this arrhythmia, since it could be applied without anæsthesia or operation and uncomplicated by the administration of any drug other than the one to be studied. We were concerned in this work primarily with a study of the irregularity produced by morphine and not with its general action on the heart.

### *Method.*

Morphine was injected in amounts from 30 to 90 mgs. in four dogs in eight experiments. The weight of the dogs was about 6 kilogrammes. In two additional experiments larger doses, in one over 2.0 g., were given.

The injections were made into one of the superficial veins of the ear or leg and were practically painless, much less so than subcutaneous injection. Care was taken that the animals were quiet some time before and during the time the records were made. The right fore limb and left hind limb were shaved and non-polarizable electrodes of the type described by Kahn<sup>7</sup> applied. These were connected with the galvanometer (Einthoven thread galvanometer, large model of Edelmann). The movements of the thread of the galvanometer were photographed in the usual way on a photographic registration apparatus. At various times during the experiment the pulse was also counted by the aid of a stop watch.

*The action of morphine on the rate and rhythm of the heart.*

In all experiments the final action of morphine was to produce a slower heart rate. In all experiments but one, irregularities of rhythm were obtained either during the full action of the drug or during recovery, occurring spontaneously or as the result of the administration of atropine. The first effect of the intravenous injection of 30 to 60 mgs. of morphine in the dog is usually an increase in pulse rate lasting from 5 to 15 minutes. The heart then becomes slower than the normal rate present before injection, but may show a similar temporary increase as a result of a second injection. The increase in pulse rate is not always associated with signs of nausea as noted by V. Egmond.<sup>2</sup> Irregularity of cardiac action may be present during the full action of the drug or the heart may be slow and regular in rate and rhythm and arrhythmia may first develop as the action of the morphine begins to wear off. In most cases it is only during partial recovery from the drug that the irregularities become most pronounced. Such recovery, so far as the heart is concerned, may be brought about at any time by the administration of 1 to 2 mg. of atropine, and, if this drug is injected subcutaneously, the complete recovery as a result of slow absorption is sufficiently delayed to allow the irregularities to be recognised and records obtained. The arrhythmia persists, of course, a much longer time during slower spontaneous recovery, and furthermore may reappear an hour or more after atropine is administered. The antagonistic action of the atropine on the heart, while complete, lasts for only a relatively short time and the heart may again return to a condition of arrhythmia or less frequently to a slow regular rate.

We have then to deal here with an action of morphine which is ultimately entirely abolished by the administration of atropine and, according to V. Egmond,<sup>2</sup> also by vagus section. We may thus conclude that the action of morphine, in producing disturbance in rhythm of the dog's heart in the amounts employed in these experiments, is due to action through the vagus mechanism and is not the result of any action on the cardiac muscle itself. The numerous electrocardiograms that we have obtained during the full action of morphine and during spontaneous recovery and recovery induced by atropine, show, we believe, that the changes in rate and rhythm of the



heart are due to the production of partial or complete sino-auricular\* and auriculo-ventricular block with the occasional occurrence of spontaneous auricular and ventricular beats.

Production of partial or complete auriculo-ventricular block by vagus stimulation has been described by a number of observers, and certain drugs, of which the most important are the members of the digitalis series, may produce this effect. Since records of the contraction of the auricle and ventricle obtained with open thorax or by means of the venous pulse or the electrocardiogram give no direct indication of the activity of the sinus region, any evidence of blocking of the cardiac impulse between the sinus and the auricle is indirect. If an auricular rhythm is suddenly halved, or if at times there is a dropped auricular beat in an otherwise regular auricular rhythm, the result may be explained in one of two ways. It may be supposed that the portion of the heart in which the cardiac impulse normally arises, represented probably by the sinus region, begins suddenly to discharge at half its normal rate or sometimes fails to discharge at its regular interval, or as a second possibility we may assume the development of a disturbance in the conducting path from the sinus to the auricle so that only every other impulse passes over this path and affects the auricle (2 : 1 S-A block). In other cases only every third or every fourth impulse is conducted, or when the disturbance is less pronounced only an occasional impulse may be blocked. The latter is the usual interpretation applied by analogy with the auriculo-ventricular conducting system. That such disturbance in conduction between the auricle and ventricle does occur has been conclusively proven, and in these cases the ventricular beat bears a relation to the auricular beat such as is presumed to exist between the recorded auricular beat and the unrecorded sinus beat in the condition of sino-auricular block. With these facts as criteria, sino-auricular block has been described as a result of injury to or traction on the sinus region of the mammalian heart by Hering<sup>4</sup> and by Erlanger and Blackman,<sup>3</sup> in clinical cases of heart disease by Mackenzie,<sup>8</sup> Joachim,<sup>6</sup> Wenckebach,<sup>11</sup> Hewlett,<sup>4</sup> and Riebold,<sup>10</sup> and after the experimental administration of aconitine by Cushny.<sup>1</sup> A full discussion of the subject is given in the paper of Riebold.<sup>10</sup>

---

\* Several recent writers have expressed doubt that a condition of sino-auricular block, as comparable in any way to auriculo-ventricular block, can be considered as possible in the mammalian heart. Wybauw<sup>12</sup> thinks this condition cannot be assumed to exist because of the brief interval between the activity of the sinus region and the right auricle. Magnus-Alsleben<sup>9</sup> denies the importance that recent work has ascribed to the sinus region and finds that a gradual transition of automaticity or capacity for impulse formation is present throughout the sino-auricular and auricular regions. On these grounds he denies the presence of any mechanism comparable to the auriculo-ventricular conduction system and hence the possibility that sino-auricular block can occur. In a series of experiments which will be published later, we have determined the period of conduction of the electrical condition from the sinus region to the right auricle, and find that in the dog it varies between 0.02 and 0.03 sec.. The auriculo-ventricular conduction time in the same animals was from 0.07 to 0.10 sec.. While the S-A conduction time is thus only about one fourth that of the A-V conduction time, the impulse is nevertheless delayed in this region in an exactly comparable way to its delay in the auriculo-ventricular conducting system.

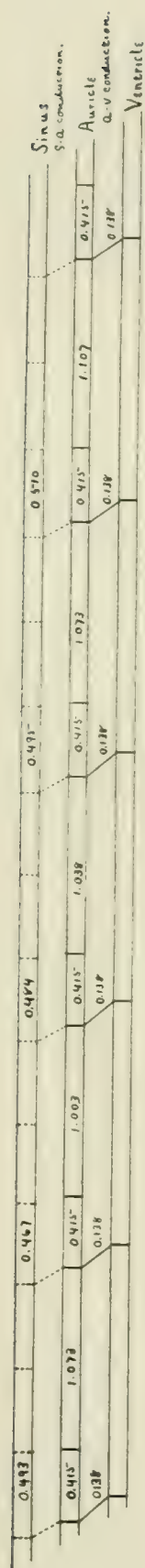


Fig. 1.

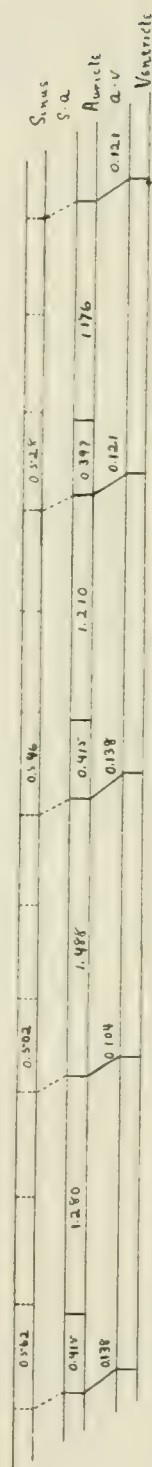


Fig. 2.

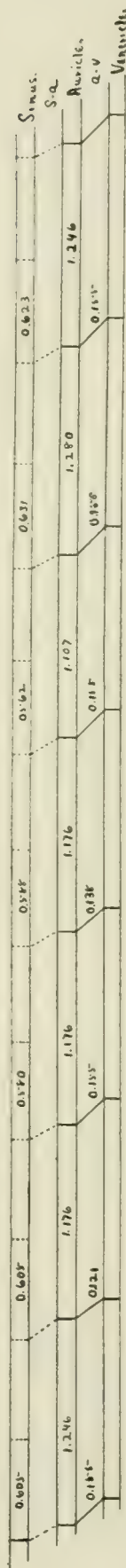


Fig. 3.

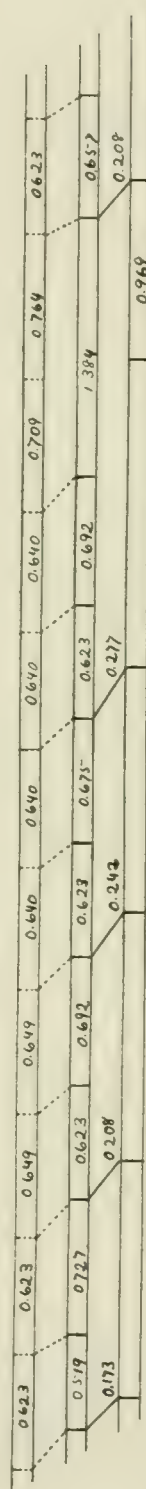


Fig. 4.

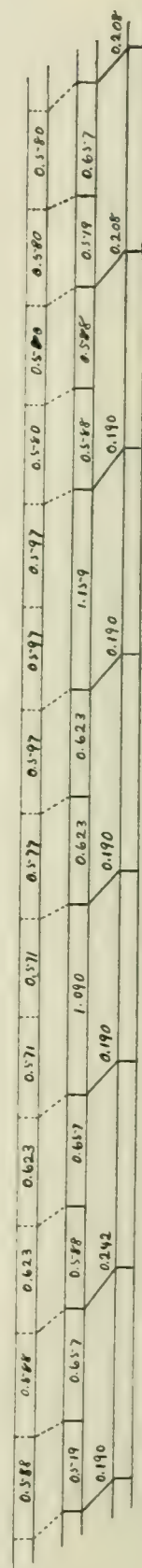


Fig. 5.



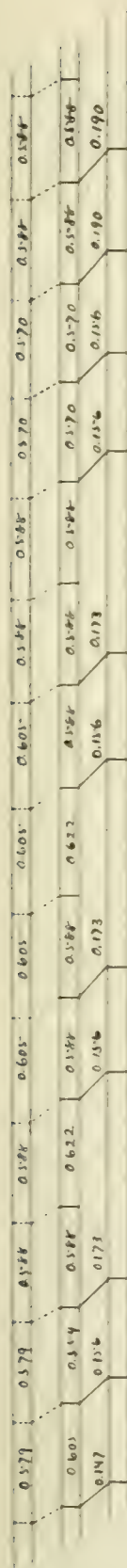


Fig. 6.

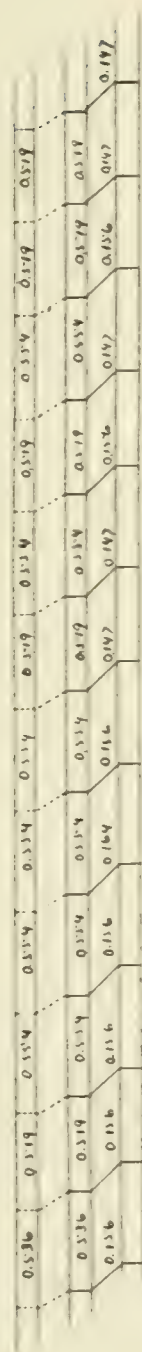


Fig. 7.

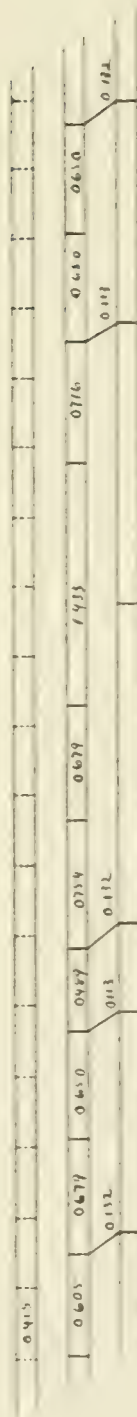


Fig. 10.

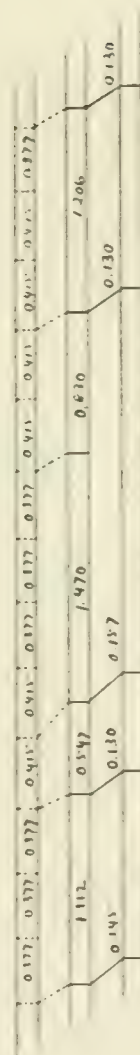


Fig. 11.

In Figures 1 to 7, the cardiac rhythm under the full action of morphine, and the recovery stages following the administration of atropine in the course of one experiment, are shown. Between the two lowest lines the beat of the ventricle, between the two middle lines the auricular beat, is represented; and the line connecting the two represents the rate of auriculo-ventricular conduction. The figures give the time of separation of the auricular beats and the time of *A-V* conduction. These were measured from the record and the charts plotted. Between the two top lines is represented (in dotted lines) the probable activity of the sinus region as inferred from the auricular and ventricular rhythm. The general assumption is that the sinus rate is represented by the auricular rate after all influence of the morphine action through the vagus is removed by the administration of atropine. Assuming this to be true, the action of morphine and the stages of recovery can all be explained by different degrees of sino-auricular and auriculo-ventricular block. Fig. 1 shows a ventricular rate of about 41 per minute fifty minutes after two intravenous injections of 30 mgs. each of morphine sulphate. One minute before Fig. 2, 0.5 mgs. of atropine sulphate was injected subcutaneously. Fig. 3, 4 and 5 follow in two, four and four minutes respectively. A second administration of 0.5 mg. of atropine was made after Fig. 5, and Fig. 6 and 7 represent the rhythm in the next three minutes. Fig. 8 is an electrocardiogram showing partial sino-auricular and auriculo-ventricular block. Fig. 9 is from the same experiment after complete recovery had occurred as a result of the administration of atropine. Fig. 10 is interpreted as a condition of complete sino-auricular block occurring after the administration of 180 mgs. of morphine in another experiment. The auricular rate following recovery showed intervals of 0.415 seconds. A record taken a short time before the one charted in Fig. 10, and shown in Fig. 11, is apparently a partial *S-A* and *A-V* block.\* These last two records are examples of irregularities occurring under the full action of morphine.

According to our interpretation the action of morphine on the heart through the vagus mechanism is to produce a loss or impairment of conduction between the auricle and ventricle and between the point of origin of the impulse and the auricle. In partial block very long intervals in which conduction is depressed, may lead to the development of independent auricular or ventricular beats. The slow regular pulse which is observed in most cases for some time after the administration of morphine is apparently that of combined *S-A* and *A-V* block of partial and regular character. In such a condition every alternate, every third, fourth or fifth impulse originating in the sinus region ultimately reaches the ventricle and the pulse

---

\* Another possible interpretation of Fig. 1 and the subsequent figures, suggested to the writers by Dr. Hewlett, is the assumption of a somewhat more rapid sinus rate: approximately 0.37 sec.. This has the advantage of rendering unnecessary the assumption of spontaneous or premature auricular beats in Fig. 1 and 2. According to this interpretation, Fig. 1 would represent a condition in which every third and fourth sinus impulse was blocked; Fig. 2 would represent a similar condition, except that in the second auricular cycle the condition would be one of 4:1 *S-A* block, and Fig. 3 a condition of 3:1 *S-A* block.



is slow but regular. In some cases the character of the block is less regular and the ventricular rhythm is irregular. During recovery from the morphine the irregularities are as a rule more frequent and more pronounced, associated with a gradual removal of the condition of depressed conductivity and a loss of the characteristic of a regular 2:1, 3:1, 4:1 or 5:1 block. The depression of conductivity is most pronounced between the sinus region and the auricle, but usually there is also a certain degree of auriculo-ventricular block. The sino-auricular system recovers its normal conductivity after the administration of atropine as a rule before the auriculo-ventricular system. It is also apparently the first to be affected by the morphine.

In one experiment we administered 180 mg. of morphine within one hour and in another 2.2 g. in the course of 4 hours with similar results as in the other experiments. The animal in the last experiment went into a condition of great reflex excitability with short tetanic convulsions, but at no time was any greater action on the rhythm of the heart observed than that present after much smaller doses. As in the case of the other experiments the action on the rhythm and rate of the heart was completely antagonized by a small dose (2.0 mg.) of atropine.

TABLE I.

EFFECT OF MORPHINE AND ATROPINE ON THE ELECTROCARDIOGRAM.

| EXP. | NORMAL. |    |    |   |    |       | AFTER MORPHINE. |   |    |   |    |       | AFTER ATROPINE. |    |    |   |      |       |
|------|---------|----|----|---|----|-------|-----------------|---|----|---|----|-------|-----------------|----|----|---|------|-------|
|      | P       | Q  | R  | S | T  | RT    | P               | Q | R  | S | T  | RT    | P               | Q  | R  | S | T    | RT    |
| 6    | 3       | 6  | 25 | 6 | -7 | 0.192 | 1.5             | 2 | 19 | 6 | +6 | 0.227 | 2               | 3  | 16 | 5 | 2    | 0.21  |
| 7    | 3       | 14 | 27 | 0 | 5  | 0.240 | 2               | 8 | 28 | 0 | -1 | 0.280 | 3.5             | 11 | 28 | 0 | 5    | 0.25  |
| 8    | 2       | 9  | 33 | 6 | +2 | 0.207 | 1               | 6 | 30 | 6 | +2 | 0.235 | 2               | 6  | 25 | 6 | +0.5 | 0.21  |
| 9    | 3       | 8  | 30 | 6 | -4 | 0.185 | 0.5             | 6 | 24 | 5 | +3 | 0.235 | 0.5             | 5  | 18 | 5 | -0.5 | 0.175 |
| 10   | 2       | 6  | 25 | 6 | -2 | 0.243 | 1               | 2 | 19 | 6 | +3 | 0.262 | 2               | 2  | 16 | 7 | +3   | 0.188 |

*Effect of morphine on the electrocardiogram.*

Table 1 shows the changes in the size of the waves of the electrocardiogram accompanying the action of morphine and atropine in five experiments. In each case the measurements (in millimetres) represent averages of a number of cycles. From this table it may be seen that morphine causes (a) a marked reduction in the size of the *P* and *Q* waves and a smaller and less constant reduction of the *R* wave, (b) no effect on the *S* wave, (c) an increase in the size of the *T* wave, when this is normally positive, a change to a positive *T* when this wave was normally negative, and finally an increase in the length of systole of the ventricle as recorded from the beginning of the *R* wave to the end of the *T* wave. Atropine tends to restore the *P* wave to normal, has little effect on *Q* and still further decreases *R*. It likewise does not affect the *S* wave. The *T* wave under atropine tends to return to the condition present before the administration of morphine and the systole is also shortened (interval from *R* to end of *T* waves).

## SUMMARY.

1. The unanæsthetized dog shows, under the influence of intravenous and subcutaneous administration of morphine, irregularity in cardiac action. The heart rate is also retarded. Electrocardiographic records indicate that the slowing and arrhythmia are due to disturbance of conduction between the point of origin of the cardiac impulse and the auricle and between the auricle and ventricle.

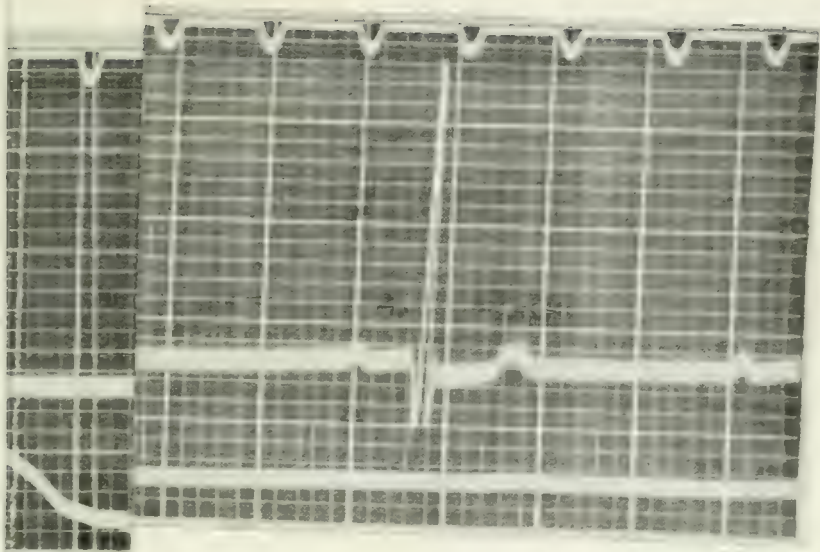
2. This effect of morphine is antagonized by atropine. During recovery, transition stages from partial sino-auricular and auriculo-ventricular heart-block to a condition of normal conductivity may be recognized.

3. Certain changes in the electrocardiogram under the action of morphine and atropine are described. These indicate (1) a decrease in extent of auricular contraction (reduction of *P* wave) and (2) an increase in the duration (*R-T* interval) and probably in the extent (size of positive *T* wave) of systole.

## BIBLIOGRAPHY.

- <sup>1</sup> CUSHNY. *Heart*, 1910, I, 1.
- <sup>2</sup> EGMOND (V.). *Archiv. f. exper. Pathol. u. Pharmakol.*, 1911, LXV, 197.
- <sup>3</sup> ERLANGER AND BLACKMAN. *Amer. Journ. of Physiol.*, 1907, XIX, 125.
- <sup>4</sup> HERING. *Zeitschr. f. exper. Pathol. u. Therap.*, 1906, III, 511.
- <sup>5</sup> HEWLETT. *Journ. Amer. med. Assoc.*, 1907, XLVIII, 47.
- <sup>6</sup> JOACHIM. *Deutsch. Archiv f. klin. Med.*, 1905, LXXXV, 373.
- <sup>7</sup> KAHN. *Archiv f. d. ges. Physiol.*, 1909, CXXVI, 197.
- <sup>8</sup> MACKENZIE. *Brit. med. Journ.*, 1902, II, 1411.
- <sup>9</sup> MAGNUS-ALSLEBEN. *Archiv. f. exper. Pathol. u. Pharmakol.*, 1911, LXIV, 228.
- <sup>10</sup> RIEBOLD. *Zeitschr. f. klin. Med.*, 1911, LXXIII, 1.
- <sup>11</sup> WENCKEBACH. *Archiv. f. Anat. u. Physiol., Physiol. Abth.*, 1906, 297, and 1907, 1.
- <sup>12</sup> WYBAUW. *Archiv. internat. de Physiol.*, 1910, x, 79.





ig. 8.  
*R* at  
fifth

ig 9.  
The

| 日期         | 姓名     | 性别 | 年龄  | 籍贯  | 职业 | 文化程度 | 健康状况 | 婚姻状况 | 宗教信仰 | 政治面貌 | 备注 |
|------------|--------|----|-----|-----|----|------|------|------|------|------|----|
| 1945.12.1  | 张三     | 男  | 25  | 山西  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.2  | 李四     | 女  | 22  | 河北  | 学生 | 初中   | 健康   | 未婚   | 无    | 团员   |    |
| 1945.12.3  | 王五     | 男  | 30  | 山东  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.4  | 赵六     | 女  | 28  | 河南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.5  | 孙七     | 男  | 35  | 浙江  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.6  | 周八     | 女  | 32  | 江苏  | 医生 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.7  | 吴九     | 男  | 40  | 安徽  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.8  | 郑十     | 女  | 38  | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.9  | 冯十一    | 男  | 45  | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.10 | 陈十二    | 女  | 42  | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.11 | 林十三    | 男  | 48  | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.12 | 黄十四    | 女  | 45  | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.13 | 刘十五    | 男  | 50  | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.14 | 周十六    | 女  | 48  | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.15 | 吴十七    | 男  | 52  | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.16 | 郑十八    | 女  | 50  | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.17 | 冯十九    | 男  | 55  | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.18 | 陈二十    | 女  | 52  | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.19 | 林二十一   | 男  | 58  | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.20 | 黄二十二   | 女  | 55  | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.21 | 刘二十三   | 男  | 60  | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.22 | 周二十四   | 女  | 58  | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.23 | 吴二十五   | 男  | 62  | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.24 | 郑二十六   | 女  | 60  | 辽宁  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.25 | 冯二十七   | 男  | 65  | 黑龙江 | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.26 | 陈二十八   | 女  | 62  | 河北  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.27 | 林二十九   | 男  | 68  | 山西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.28 | 黄三十    | 女  | 65  | 山东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.29 | 刘三十一   | 男  | 70  | 河南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.30 | 周三十二   | 女  | 68  | 江苏  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1945.12.31 | 吴三十三   | 男  | 72  | 安徽  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.1   | 郑三十四   | 女  | 70  | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.2   | 冯三十五   | 男  | 75  | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.3   | 陈三十六   | 女  | 72  | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.4   | 林三十七   | 男  | 78  | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.5   | 黄三十八   | 女  | 75  | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.6   | 刘三十九   | 男  | 80  | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.7   | 周四十    | 女  | 78  | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.8   | 吴四十一   | 男  | 82  | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.9   | 郑四十二   | 女  | 80  | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.10  | 冯四十三   | 男  | 85  | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.11  | 陈四十四   | 女  | 82  | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.12  | 林四十五   | 男  | 88  | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.13  | 黄四十六   | 女  | 85  | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.14  | 刘四十七   | 男  | 90  | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.15  | 周四十八   | 女  | 88  | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.16  | 吴四十九   | 男  | 92  | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.17  | 郑五十    | 女  | 90  | 辽宁  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.18  | 冯五十一   | 男  | 95  | 黑龙江 | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.19  | 陈五十二   | 女  | 92  | 河北  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.20  | 林五十三   | 男  | 98  | 山西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.21  | 黄五十四   | 女  | 95  | 山东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.22  | 刘五十五   | 男  | 100 | 河南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.23  | 周五十六   | 女  | 98  | 江苏  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.24  | 吴五十七   | 男  | 102 | 安徽  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.25  | 郑五十八   | 女  | 100 | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.26  | 冯五十九   | 男  | 105 | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.27  | 陈六十    | 女  | 102 | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.28  | 林六十一   | 男  | 108 | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.29  | 黄六十二   | 女  | 105 | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.30  | 刘六十三   | 男  | 110 | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.1.31  | 周六十四   | 女  | 108 | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.1   | 吴六十五   | 男  | 112 | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.2   | 郑六十六   | 女  | 110 | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.3   | 冯六十七   | 男  | 115 | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.4   | 陈六十八   | 女  | 112 | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.5   | 林六十九   | 男  | 118 | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.6   | 黄七十    | 女  | 115 | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.7   | 刘七十一   | 男  | 120 | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.8   | 周七十二   | 女  | 118 | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.9   | 吴七十三   | 男  | 122 | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.10  | 郑七十四   | 女  | 120 | 辽宁  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.11  | 冯七十五   | 男  | 125 | 黑龙江 | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.12  | 陈七十六   | 女  | 122 | 河北  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.13  | 林七十七   | 男  | 128 | 山西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.14  | 黄七十八   | 女  | 125 | 山东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.15  | 刘七十九   | 男  | 130 | 河南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.16  | 周八十    | 女  | 128 | 江苏  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.17  | 吴八十一   | 男  | 132 | 安徽  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.18  | 郑八十二   | 女  | 130 | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.19  | 冯八十三   | 男  | 135 | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.20  | 陈八十四   | 女  | 132 | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.21  | 林八十五   | 男  | 138 | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.22  | 黄八十六   | 女  | 135 | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.23  | 刘八十七   | 男  | 140 | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.24  | 周八十八   | 女  | 138 | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.25  | 吴八十九   | 男  | 142 | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.26  | 郑九十    | 女  | 140 | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.27  | 冯九十一   | 男  | 145 | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.28  | 陈九十二   | 女  | 142 | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.29  | 林九十三   | 男  | 148 | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.2.30  | 黄九十四   | 女  | 145 | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.1   | 刘九十五   | 男  | 150 | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.2   | 周九十六   | 女  | 148 | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.3   | 吴九十七   | 男  | 152 | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.4   | 郑九十八   | 女  | 146 | 辽宁  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.5   | 冯九十九   | 男  | 155 | 黑龙江 | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.6   | 陈一百    | 女  | 146 | 河北  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.7   | 林一百一   | 男  | 154 | 山西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.8   | 黄一百二   | 女  | 150 | 山东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.9   | 刘一百三   | 男  | 156 | 河南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.10  | 周一百四   | 女  | 152 | 江苏  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.11  | 吴一百五   | 男  | 158 | 安徽  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.12  | 郑一百六   | 女  | 154 | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.13  | 冯一百七   | 男  | 160 | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.14  | 陈一百八   | 女  | 156 | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.15  | 林一百九   | 男  | 162 | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.16  | 黄一百十   | 女  | 158 | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.17  | 刘一百一十  | 男  | 164 | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.18  | 周一百一十一 | 女  | 162 | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.19  | 吴一百一十二 | 男  | 166 | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.20  | 郑一百一十三 | 女  | 160 | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.21  | 冯一百一十四 | 男  | 168 | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.22  | 陈一百一十五 | 女  | 162 | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.23  | 林一百一十六 | 男  | 170 | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.24  | 黄一百一十七 | 女  | 165 | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.25  | 刘一百一十八 | 男  | 172 | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.26  | 周一百一十九 | 女  | 168 | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.27  | 吴一百二十  | 男  | 174 | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.28  | 郑一百二十一 | 女  | 166 | 辽宁  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.29  | 冯一百二十二 | 男  | 178 | 黑龙江 | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.30  | 陈一百二十三 | 女  | 168 | 河北  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.3.31  | 林一百二十四 | 男  | 176 | 山西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.1   | 黄一百二十五 | 女  | 170 | 山东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.2   | 刘一百二十六 | 男  | 178 | 河南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.3   | 周一百二十七 | 女  | 172 | 江苏  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.4   | 吴一百二十八 | 男  | 180 | 安徽  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.5   | 郑一百二十九 | 女  | 174 | 湖北  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.6   | 冯一百三十  | 男  | 182 | 湖南  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.7   | 陈一百三十一 | 女  | 176 | 四川  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.8   | 林一百三十二 | 男  | 184 | 江西  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.9   | 黄一百三十三 | 女  | 178 | 广东  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.10  | 刘一百三十四 | 男  | 186 | 广西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.11  | 周一百三十五 | 女  | 180 | 福建  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.12  | 吴一百三十六 | 男  | 188 | 贵州  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.13  | 郑一百三十七 | 女  | 182 | 云南  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.14  | 冯一百三十八 | 男  | 190 | 陕西  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.15  | 陈一百三十九 | 女  | 184 | 甘肃  | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.16  | 林一百四十  | 男  | 192 | 宁夏  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.17  | 黄一百四十一 | 女  | 186 | 青海  | 教师 | 大学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.18  | 刘一百四十二 | 男  | 194 | 新疆  | 商人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.19  | 周一百四十三 | 女  | 190 | 内蒙古 | 工人 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.20  | 吴一百四十四 | 男  | 198 | 吉林  | 农民 | 小学   | 健康   | 已婚   | 无    | 党员   |    |
| 1946.4.21  | 郑一百四十五 | 女  | 192 | 辽宁  | 教师 | 大学   | 健康   |      |      |      |    |



## TWO MODES OF CLOSURE OF THE HEART VALVES.

BY YANDELL HENDERSON AND F. ELMER JOHNSON.

(*From the Physiological Laboratory of the Yale Medical School*).

It is universally believed that in the normal heart the valves operate so perfectly that in closing they allow no leak whatever,—not the smallest fraction of a drop. As the cause of their closure it is customary to allege the occurrence of a back pressure, yet it is self evident that if this is the cause the valves must leak in closing.

Imagine a door standing open between two rooms. Imagine the door being slammed in one's face by wind from the other room. Does not one always feel a strong draught of air through the lessening space and in front of the swinging surface as it closes? In such a closure there is necessarily a huge leak. Practically all valves in machinery which are closed by a back pressure have a greater or less leakage. In fact it is the regurgitation which causes the closure.

The literature of this subject is too well-known to need extended review.

It was held by Krehl<sup>9</sup> that while blood is flowing through the ostia of the heart eddies form in the sinuses at the back of the valve flaps. When the flow ceases these eddies are supposed to open out like tightly-wound clock springs and throw the valve flaps into approximation. Thus, when a higher pressure develops an instant later, the valves become tightly closed without leakage.

These eddies certainly occur, and they are important in preventing the flaps from being pressed back flat against the ventricular or arterial walls. But they are not otherwise an essential part of the mechanism of closure, for, as we shall show, the valves will close almost equally well without them. It is certainly true that the heart valves *may* close without the slightest leak. This was shown seventy years ago by Baumgarten<sup>1</sup> who cut away the auricles, tied the aorta, and directed a jet of water through the mitral valve. When the jet was suddenly shut off, the valve closed instantly. The heart could then be inverted without the slightest leakage.

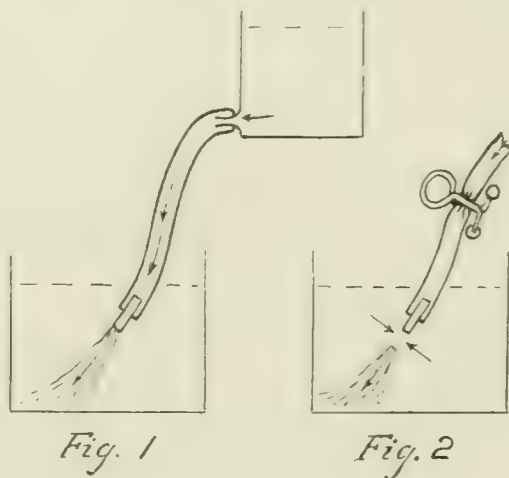
In this experiment the valve is closed by the pressure produced within the ventricle by the inertia of the jet. It is essential to remember, however, that this pressure is not of the static variety. It is kinetic. It is like the increased strain against, and simultaneously also away from, a sea-wall as a wave rises against it. This conception is without doubt mechanically correct. So far as we are aware it is universally accepted. It is, however, for many minds (our own included) more or less intangible. It has therefore seemed to us more convenient, and perhaps also truer, to assign the closure

of the heart valves, not to a momentarily unbalanced kinetic pressure, but rather to certain events of an easily visualized sort which always accompany it. Their central feature may be denominated as *the breaking of a jet at an ostium*.

This is, we believe, essentially the same conception as that of Ceradini.<sup>2</sup> He first pointed out that the closure of the heart valves depends normally not upon a static back pressure, and not upon eddies, in the sense of Krehl, but upon something which happens at the instant when the flow through an ostium ceases. It appears to us, however, that few modern writers have grasped exactly the idea which Ceradini meant to convey. While the distinction between the "breaking jet" and the "back pressure" conception of valve closure is not of much importance in relation to the normal heart, it is essential for the explanation of certain abnormal phenomena.

*The breaking of a jet at an ostium.*

Through any relatively small opening, let fluid be discharged into a large chamber containing more of the same liquid. A syringe with its nozzle dipped in a bucket of water affords such conditions. Let the discharge suddenly cease. The fluid remaining behind the opening (*i.e.*, in the syringe) comes to a sudden standstill. Beyond the opening, however, the column of fluid which has already been discharged continues moving straight forward through the mass of liquid in the large chamber, *i.e.*, the bucket. Thus at the instant when the discharge ceases the jet of fluid *breaks* at the opening. The forward movement of the column leaves in its rear a small area of negative pressure. This area is analagous to the wake of a ship. Into it from each side fluid is drawn. *It is the lateral inrush into the wake of the breaking jet just beyond the ostium which, according to our view, is normally the cause of the closure of the heart valves.*

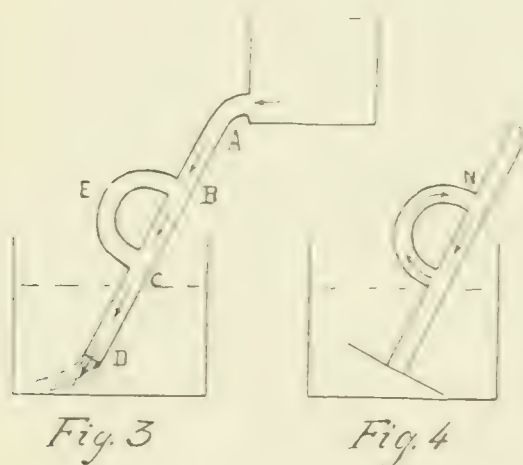


The mechanics of this process are shown by the following experiments. A reservoir of water coloured with some dye was placed on a high shelf. From this reservoir a small tube led down under the surface of clear water



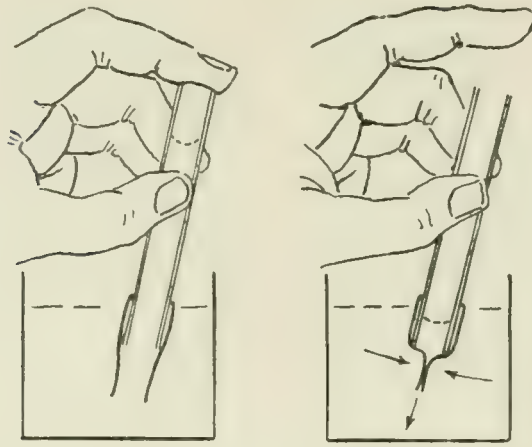
in a large glass jar. When the coloured liquid was allowed to flow, a distinct jet, as shown in Fig. 1, was visible. The flow was suddenly stopped by pinching the tube, as in Fig. 2. Instantly all movement within the tube ceased. That portion of the coloured liquid which had already passed out of the tube into the jar however did not stop. On the contrary, the coloured jet, breaking at the mouth of the tube, continued onward through the clear liquid. As the break occurred, clear liquid was drawn suddenly into the wake of the jet from around the opening of the tube. If flaps had been present, this inrush from the sides would have tended to throw them into approximation.

Another experiment which shows the breaking of the jet is illustrated in Fig. 3 and 4. Here the tube ABCD through which the fluid is allowed to flow has a byway E. So long as fluid flowed into A and escaped freely at D, the movement was as shown by the arrows in Fig. 3. The liquid in E was either entirely stationary, or else flowed slowly downward. Suddenly the opening at D was closed as in Fig. 4. Instantly every particle of liquid



in the parts of the tube marked AB and CD came to a standstill. At the same instant, however, the momentum of that part of the column between B and C induced a circulation of fluid from B to C to E and back to B. When a small piece of sheet rubber was attached to the angle N, and the experiment was repeated, the flap was thrown into the position shown by the dotted line. The experiment was repeated, but this time the tube was pinched at A. Exactly the same circulation instantly occurred. Thus it mattered not how the flow was stopped, whether by resistance in front, or by shutting off the stream from behind, the circulation round B to C to E and back to B resulted.

Still another simple experiment illustrating the lateral inflow in the wake of a jet breaking at an ostium is as follows. The top of a rubber finger stall was cut off, and the stall was then tied over the end of a glass tube a little larger than one's finger. The tube and stall were immersed in a vessel of water. A finger was applied to the uncovered end of the tube, and this end was lifted out of the water, while the end bearing the stall was still under

*Fig. 5**Fig. 6*

water. This position is shown in Fig. 5. The finger was suddenly removed. The column of water fell quickly; the discharge ceased suddenly; the jet broke at the ostium; and as the lateral inrush occurred, the walls of the stall were snapped together like a valve. When the finger stall was thin and flexible, no leak occurred. After closure of the valve, the level of the water in the tube stood somewhat lower than in the tank outside as shown in Fig. 6.

With the same tube and valve another experiment was performed. The tube was held so that the valve was a few centimetres below the surface of the water in a beaker. The valve hung open; the beaker was suddenly lifted, while the tube was held stationary. A back pressure upon the valve was thus induced and it closed. In doing so, however, it allowed a considerable regurgitation into the tube. It is particularly to be noted that in this experiment there was no breaking jet, but on the contrary a static back pressure.

#### *Experiments with excised heart valves.*

The experiments thus far described are mere illustrations. For a crucial observation, the heart valves themselves were employed. Several different methods of mounting valves from ox hearts were tried. A few observations upon a heart arranged in the manner described by Gad showed us that, in spite of the beauty of this method, it was not suited to our purpose. It affords a view of the flaps in the line of the lumen of the valve. For our purpose some mode of mounting was necessary which allowed a view of the flaps from the side.

After several failures, we found that with a little care it is quite easy to dissect out of an ox heart, and to mount for observation, a preparation of the mitral or tricuspid valve. The preparation consisted of a sufficient amount of the musculature just above the valve to allow its being tied over the end of a large tube. The ventricular walls were almost entirely cut away, except that the tops of the papillary muscles were left attached to the chordae tendineae. When not in use the preparation was kept in a preservative



fluid of water, 35 per cent. glycerin, and thymol. Preserved in this way connective tissue remains perfectly soft; and although decomposition ultimately occurs, it does not take place for several weeks even in warm weather.

The apparatus upon which the preparations were mounted consisted of a glass tube 30 cms. long, 7 cm. in diameter, and open at both ends. Around one end a brass ring was clamped. From this ring two rods extended 8 cms. beyond the end of the tube. To the ends of these rods a ring of transparent celluloid was fastened. The valve was supported tight against the end of the tube by passing stitches through the auricular musculature and around the brass ring. In a similar manner the papillary muscles were attached to the celluloid ring. The glass tube was supported in a vertical position by means of a lampstand at such a height that the valves themselves were 10 or 12 cms. below the surface of the water (distilled and containing no glycerin) in a glass jar or tank. Below the valves a mirror was placed, inclined at an angle of 45 degrees, so that the observer standing in front of the tank and looking into the mirror had a reflected view up through the lumen of the valve, while at the same time he saw the valve itself directly from the side. Owing to the difference in focal distance these mirror images, unfortunately, do not come out clearly in our photographs.

Various ways of causing movement in the valves were employed. These fall into two classes. Their differences show clearly, we believe, the hitherto unsuspected fact that *the heart valves are capable of two distinct types of movement in the act of closure.*

The crucial question to which we sought an answer was: Does a valve flap swing like a door upon its hinges, or does it close inward upon its ostium like a roll of carpet being unwound across a hole in the floor? The point of this question lies in the fact, evident from a consideration of our experiments with jets of coloured water, finger stalls, &c., that *if the valves are*

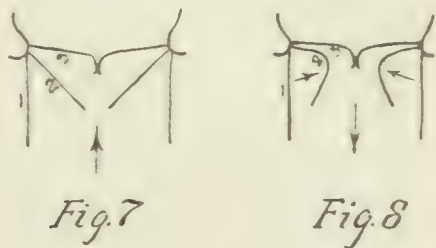


Fig. 7

Fig. 8

*closed by the breaking of a jet and a lateral inrush, then the part of the flaps nearest their base must be the first to move inward, while the edges of the flaps will be the last part to be brought into a position of closure.* In this mode of closure no leak whatever would occur. If, on the other hand, at a time when the valves are open, a back flow is started by some difference in (static) pressure, the edges of the flaps being nearest mid-channel and also thinnest and lightest will be the first part to turn inward. In such a closure a considerable regurgitation is inevitable. The distinction between these two

types of movement is illustrated in Fig. 7 and 8. Position 1 in both figures shows the flaps when open, and 3 shows them closed, while 2 exhibits the difference in the positions of their parts during closure by a breaking jet and inrolling movement (in Fig. 8), as compared with a back flow and hinge-like swing (in Fig. 7).

The differences in the conditions inducing these two modes of closure in heart valves mounted as above described were briefly as follows:—The hinge movement and a considerable regurgitation occurred when the large glass tube with the valve fastened to its end was lowered further into the water in the tank. The same type of movement and regurgitation were induced also by sucking air out of the top of the glass tube. Identical results were obtained by drawing a plunger upward through the tube. In order to obtain the regurgitative closure in any of these ways it was essential that the valve should previously have been in a state of quiescence and hanging at least partially open, or else held more widely open by a very slow downward stream. It is to be particularly noted that a back pressure probably never arises in a normally beating heart while the valves are in these positions. Such a concatenation may happen however in a heart with a dissociation of the auricular and ventricular rhythms, as will be discussed later.

On the other hand the inrolling form of closure invariably occurred under conditions simulating the movements of blood in the normal heart. Such movements were induced in two ways. (1) A weighted plunger was allowed to fall part way through the glass tube. A quick discharge followed by a sudden cessation of the discharge was thus obtained. This arrangement and the resulting movement of the valve flaps is illustrated by the photographs of the tricuspid valve in Fig. 9 to 12. (2) A large rubber stopper with a small hole cut through it was put into the top of the glass tube carrying the valve. Into this hole was fitted a smaller stopper connected with a small rubber tube. Suction was applied on this tube at the same time that the valves were held open from below by means of a hook. After the water had thus been drawn up into the large glass tube to a level 5 to 10 cms. above that in the tank it could be held air-bound in this position by pinching the small rubber tube. This procedure and its results are illustrated by the photographs of the mitral valve in Fig. 13 to 16. When everything was ready for an observation the small stopper was suddenly withdrawn. Air was thus admitted, and *the column of water fell suddenly down the glass tube and out through the valve. At the instant that the top of the column passed below the level of the water in the tank, and its further progress met resistance (the hydrostatic pressure in the tank opposing the momentum of the column and causing it to break) the inrolling closure of the flaps occurred. Thus in a most beautiful manner the valve caught the column just at the lowest level which it reached, and shut off all regurgitation so precisely that the level of fluid inside the chamber above the valve was held thereafter 2 or 3 cms. (according to the distance through which the column had fallen) below that in the tank outside.*



Fig. 9-12. Showing the inrolling

Fig. 9 shows the valve closed

Fig. 10. The plunger is falling

Fig. 11. The fall of the plunger inward. Note the bowed s

Fig. 12. An instant later. Th



Fig. 11.

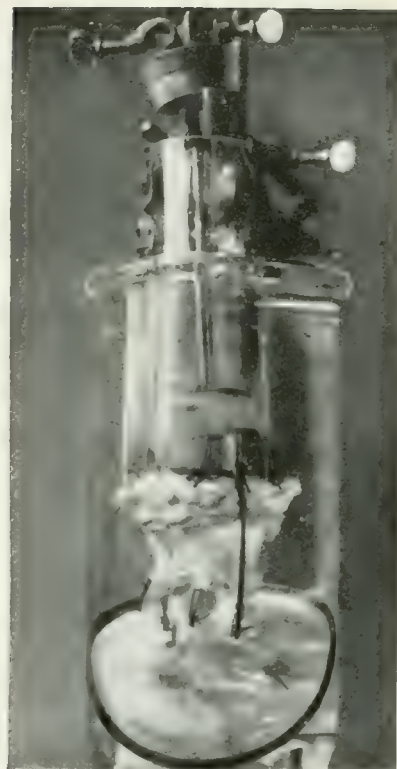


Fig. 12.

Fig. 13-16. Showing the mitra

Fig. 13 shows the valve in the c  
down.

Fig. 14. The large glass tube h  
rubber tube. During this  
has now been withdrawn a

Fig. 15. The small stopper h  
falling column of water has

Fig. 16. The column has reac  
valve flaps together, thus  
large glass tube stands belo

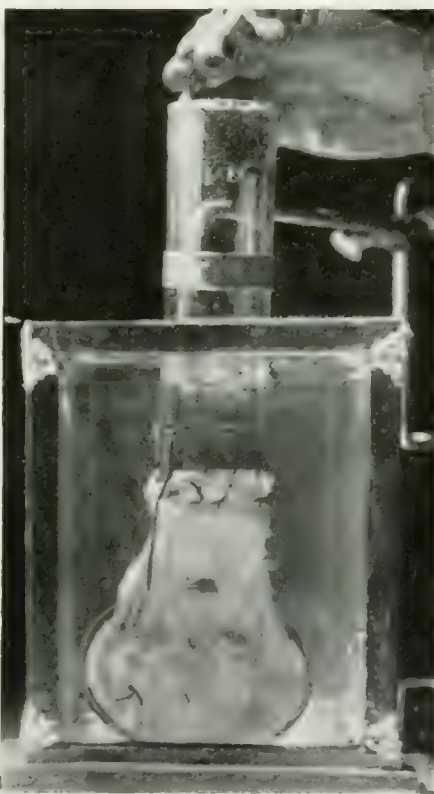


Fig. 15.

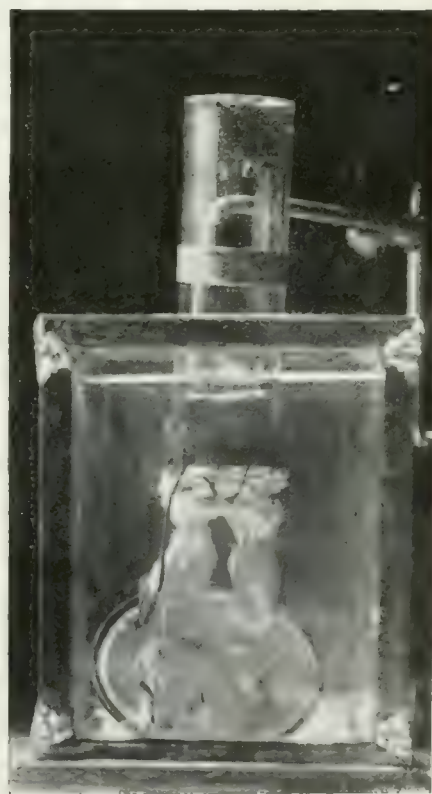
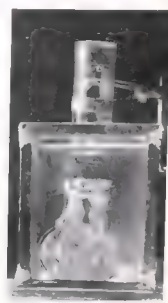
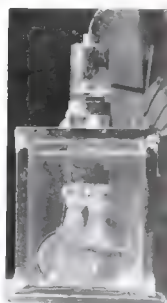
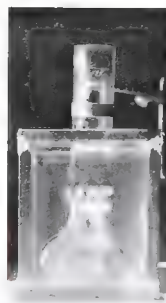


Fig. 16.





These points will be better appreciated from an examination of the photographs, herewith reproduced and of the legends accompanying them than from a general description. In particular, attention should be called to Fig. 11 in which is shown the bowed shape of one of the inrolling flaps of the tricuspid.

Eddies such as are formed in the sinuses of Valsalva occurred in not a single one of the experiments thus far described. The jar and tank were too large for them to be developed.

*Auricular systole and the closure of the atrio-ventricular valves.*

We may now consider the bearing of the breaking jet conception upon the movements of the valves in the living heart under normal conditions and in disease. As regards the semilunar valves, it appears to us that the only mechanical condition under which the hinge swing might replace the inrolling mode of closure is one of extremely low arterial pressure, much below 50 mm. Hg., and this condition is incompatible with life. All other conditions (not involving extensive structural alteration in the valves themselves) appear to afford the breaking jet.

In the closure of the atrio-ventricular valves conditions differ according to the rate of the heart beat. We shall briefly point out the character of these variations and then show how they influence the closure of the valves under normal and abnormal conditions.

By his studies upon the volume curve, Henderson<sup>6</sup> has shown that when the pulse rate is slow the refilling of the ventricles normally occurs in the first part of diastole, and that it is nearly as rapid a process as is the systolic discharge. As the process of refilling nears completion, the volume curve bends in some cases gradually, in others quite sharply, toward the horizontal, indicating a sudden lessening of the rapidity of the inflow.\* This bend in the upstroke of the volume curve separates the period ordinarily called diastole into two more or less distinct parts,—the period of rapid relaxation and refilling, and the period of rest or diastasis. In a normal, actively beating heart with good tonus, the volume curve continues to rise gradually during diastasis, indicating a continuous slight inflow of blood.†

---

\* A sharp bend at this point indicates a sudden slowing of the stream into the ventricles. This will tend to "break the jet" and throw the flaps of the atrio-ventricular valve into temporary apposition. This action produces the third heart sound according to the view of Hirschfelder<sup>7</sup> and the *h* or *b* wave in the venous pulse observed by Hirschfelder, by Thayer<sup>13</sup> and by Gibson.<sup>4</sup> These phenomena can occur only in a heart in which the diastolic relaxation is rapid, the bend abrupt, and the rate of beat slow.

† Hermann Straub<sup>12</sup> in criticising Henderson's work misrepresents him as holding that during diastasis the volume curve runs parallel to the abscissa and no blood enters the ventricles. Henderson expressly stated that this would be the case only in an extremely slowly beating heart with abnormally low tonus. Straub also imagines certain sources of error in the large tambour with which Henderson's curves were recorded. In a later paper to be published in the *American Journal of Physiology* it will be demonstrated that the tambour was so arranged as to be free from these defects. Straub, in his critical paper, concluded that Henderson's interpretation of the volume curve was in many respects erroneous. In a later paper in Pflüger's *Archiv* he has adopted Henderson's opinions on practically all of these points. Henderson has recently published in Pflüger's *Archiv* an article dealing with Straub's criticisms.

It is mainly by variations in the duration of diastasis that changes in the heart rate are effected. At rapid rates this period is cut off altogether. The volume curve then consists merely of upstrokes and downstrokes indicating that refilling and discharge succeed each other in rapid alternation with no interval of diastasis.\* Auricular systole then occurs during the period of ventricular relaxation, and of course adds whatever force it has to this process. Henderson has shown however that normally the ventricles are filled under the force of venous pressure as rapidly as they relax, and that it is only when the circulation is failing and the venous pressure has fallen that auricular systole plays any considerable part in their filling.

We return now to the topic of the movements of the atrio-ventricular valves under the influence of the currents shown by the volume curve to occur within the heart. It appears in the light of our experiments that, at rapid heart rates, when the relaxation of the ventricle is abruptly terminated by the oncoming of the next contraction, the columns of blood pouring through the mitral and tricuspid valves will break sharply. By this sudden breaking of the jets the flaps would probably be rolled inward and slammed together without allowing any regurgitation even if the auricles were entirely quiescent. An auricular systole will tend to assist in the inrolling mode of closure, when the heart beat is co-ordinate, but when such co-ordination is absent, will tend to hinder it.

Quite different are the conditions when the heart is beating slowly. In this case the ventricle, after the rapid inflow of the first part of diastole, gradually relaxes further during diastasis. To allow this the valves must hang at least partially open. *If now ventricular systole occurred without a preceding auricular contraction, the mitral and tricuspid valves would be closed by the hinge type of movement, and a very considerable regurgitation of blood from the ventricles back into the auricles would necessarily occur.* This opinion is not hypothetical. It is exactly what did occur with excised heart valves when they were lowered into the tank or when suction was applied to the upper end of the glass tube on which they were mounted.

It appears, however, that nature has specially provided that, in the normal heart, the waste of energy involved in a regurgitating closure of the atrio-ventricular valves shall never take place. From the volume curve it is clear that *when auricular systole occurs during ventricular diastasis it sends a distinct wave over the ventricle, but does not cause any considerable increase in its volume.* This is shown by the fact that the curve sometimes rises considerably at this time but (in a normally beating heart) immediately falls again practically to the level at which it was prior to the auricular

---

\* In extreme tachycardia the refilling is so much reduced both in duration and volume, and the tonus of the ventricle becomes so intense that the condition called by Wenckebach "Propfung" or stoppering results. Wenckebach<sup>14</sup> regards this condition as due to the occurrence of auricular systole while the ventricle is still contracted. In Henderson's experiments it was evident that the principal factor was rather the incompleteness of the diastolic relaxation of the ventricle. The two explanations are, however, not mutually exclusive, and doubtless both factors play a part.



contraction.\* Accordingly Henderson suggested that the principal mechanical function of auricular systole is that in the slowly beating heart *the currents in the blood within the ventricle induced by the auricular wave cause the closure of the atrio-ventricular valves before the onset of ventricular systole.*

In order to test whether a slight but sudden impulse such as auricular systole imparts to the blood is capable of closing the valves we made use of the mitral preparation under the conditions shown in Fig. 13. The level of the water inside the large glass tube was at the same height as in the tank. The flaps hung partially open. The experimenter now placed his mouth a few centimetres above the upper opening of the large glass tube, but not against it, and blew his breath in a sudden puff down the tube. The puff needed but little force. It was necessary, however, that it should be sudden. If the water in the tube were quickly pushed downward even 8 or 10 mm., and then stopped by the static back pressure of the water in the tank, the effect upon the valve was striking. The flaps suddenly rolled inward and closed the ostium. It is particularly noteworthy that after this "auricular systole" had thus closed the valve the level of the water in the tube was only 5 or 6 mm. lower than at the beginning of the experiment. The wave sent into the "ventricle" (*i.e.*, the tank) had induced in its wake as it passed through the valve opening a region of negative pressure sufficient to throw the flaps into apposition, although the volume of the jet injected and broken was insignificant. It is to be noted also that, owing to the size of the tank in which the valve was immersed, there were no eddies.

There are a number of ways in which the movement of a valve flap under the influence of a wave may be illustrated. One of the simplest is that shown in Fig. 17. The arrangement consists of a narrow, shallow, but rather long pan filled with water. On the bottom near the middle a transverse strip of wood is fastened and to this a flap of oiled silk or thin sheet rubber is tacked. Threads passed through the free edge of the flap serve as *chordae tendineae* and are connected to another fixed transverse strip of wood, *i.e.*, "a papillary muscle" at the "ventricular" end of the pan (to the right). To do the experiment the hand, with the fingers slightly flexed, is dipped into the water at the "auricular" end of the pan, and is suddenly moved 4 or 5 cms. toward the valve. This "auricular systole" sends a wave down over the "ventricular" end of the pan. Immediately the valve flap rolls upward into the closed position. Unless "chordae tendineae" are present it will roll right back into the "auricle."

It is to be particularly noted that in this experiment the volume of fluid in the "ventricular" end of the pan is no greater after "auricular systole" than before. The sole effect of the wave is to close the valve. The importance of this closure is seen at once if a ventricular systole is imitated by lifting the "ventricular" end of the pan. If there has been no "auricular systole" just previously, a considerable flow from the "ventricular" to the

---

\* This point holds true also in Straub's curves,

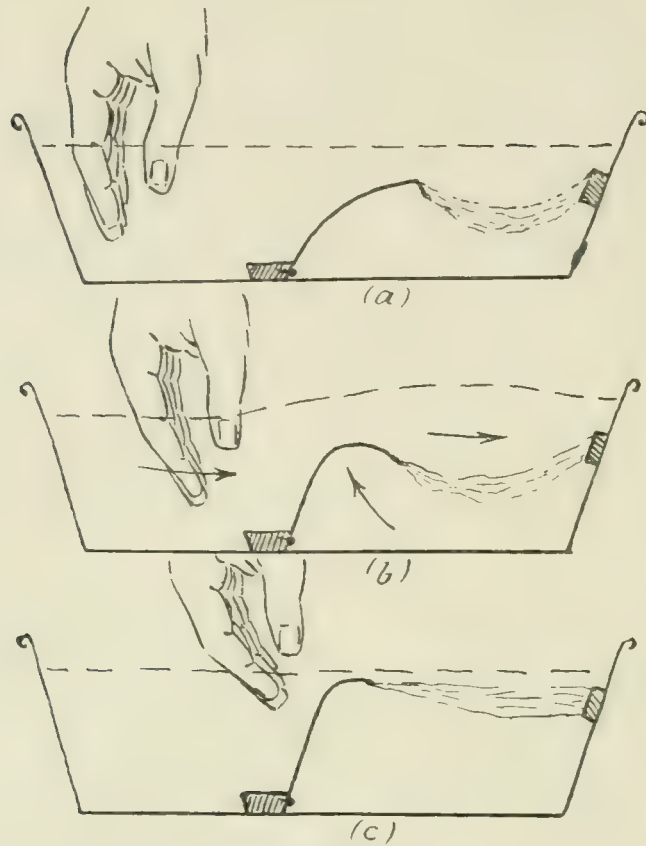


Fig. 17

“auricular” end occurs before the valve swings tight. If, however, there has been an “auricular systole,” the closed and taut valve holds the fluid in the ventricular end, and prevents this leak into the “auricle.”

Some of the data contained in a recent paper by Gesell<sup>3</sup> seem to us to be interpretable in general conformity with this view of the function of auricular systole. Gesell induced in the exposed heart of the dog various forms and degrees of dissociation between the auricular and ventricular rhythms. He estimated the influence of these conditions upon the efficiency (*i.e.*, output) of the heart by measurements of arterial pressure. He found that arterial pressure varied according to the time in the ventricular cycle at which auricular systole occurred. It was least when auricle and ventricle contracted simultaneously. It increased as auricular systole fell later in ventricular diastole and diastasis, and it reached a maximum when the auricular contraction came at its normal time, *i.e.*, just before that of the ventricle.

Gesell regarded his demonstration of these points as evidence that, contrary to Henderson's view, auricular systole normally injects a considerable quantity of blood into the ventricle. It appears to us that his observations would be adequately explained on the assumption that when auricular systole is eliminated altogether (*e.g.*, in experimental auricular fibrillation) or falls at an abnormal time in the rhythm of a slowly beating ventricle, the atrio-ventricular valves are closed by the hinge movement. Whenever this form of closure occurs, a considerable regurgitation into the auricle must



accompany it. The systolic discharge into the arteries must be correspondingly lessened, and arterial pressure lowered.\*

### *Conclusions.*

The heart valves, and particularly the atrio-ventricular valves, are capable of closing in two distinct ways.

Whenever the flow of blood through an ostium ceases abruptly, no matter whether it be because of cessation of the push from behind or because of increased resistance in front, the jet breaks. The part of the column back of the opening stops. The part which has already passed the opening continues to move straight forward. The momentum of this forward movement produces in the rear of the column a small area of negative pressure. This area is analogous to the wake of a ship. Into it fluid is drawn from each side, and this lateral inrush carries the valve flaps into a position of approximation. The part of the valve flaps nearest their base is the first to move inward, and the edges are the last part to be brought into the position of closure. In this inrolling mode of closure no regurgitation occurs.

The other type of movement occurs whenever a valve is closed by a static back pressure. It swings the flaps upon their bases like doors upon their hinges so that their edges are the first portion to approach one another. This mode of closure necessarily involves more or less, and sometimes a very large, regurgitation or leakage of blood while the flaps are swinging into position.

It is probable that the semilunar valves are always closed by the breaking jet and inrolling movement and never by the hinge swing. The eddies in the sinuses behind the valves are important in holding the flaps away from the walls, but they are otherwise unimportant in the mechanics of closure.

In the normally co-ordinated heart the occurrence of auricular systole immediately before the ventricular contraction assures the inrolling and non-leaking mode of closure in the mitral and tricuspid valves even when the rate of beat is slow. When the rate of beat is sufficiently rapid so that ventricular contraction follows immediately upon the period of rapid relaxation these valves would probably be closed by the breaking jet and inrolling movement even if no auricular systole occurred. When the rate of heart beat is slow however ventricular systole is preceded by a considerable period of diastasis, during which these valves hang open. The onset of the ventricular contraction under such conditions without a preceding auricular systole would cause their closure by the hinge type of movement and would involve a considerable regurgitation of blood into the auricles. The efficiency of the heart action would be thus considerably diminished.

---

\* The arterial pressures reported by Gesell show that in many of his experiments the circulation was failing at the time when his observations were taken. Henderson expressly stated that in a failing circulation (with insufficient venous pressure) auricular systole may inject a very considerable quantity of blood into the ventricles.

In order to induce the inrolling and non-leaking closure of the valves it is not necessary that auricular systole should inject any considerable quantity of blood into the ventricle. Henderson has shown that in a vigorous heart supplied by a normal venous pressure the ventricles are filled rapidly in the early part of diastole. At rates of beat in which auricular systole comes after this period of refilling it causes little, if any, increase in the volume of the ventricles. It sends a wave over the blood in the ventricles without causing any considerable onflow. Our experiments show that the passage of this wave is adequate to produce conditions analogous to those of a breaking jet, and thus to induce the inrolling and non-leaking closure of the mitral and tricuspid valves.

## BIBLIOGRAPHY.

- <sup>1</sup> BAUMGARTEN. *Archiv f. Anat. u. Physiol.*, 1843, 464-466.
- <sup>2</sup> CERADINI. "Der Mechanismus der halbmondförmigen Herzklappen," Leipzig, 1872, 34-45  
(Republished in Italian in Vol. II of his Opera, Milan, 1906).
- <sup>3</sup> GESELL. *Amer. Journ. of Physiol.*, 1911-12, xxix, 32-63.
- <sup>4</sup> GIBSON. *Lancet*, 1907, II, 1380.
- <sup>5</sup> GRIFFITH. *Heart*, 1912, III, 145 and 158.
- <sup>6</sup> HENDERSON. *Amer. Journ. Physiol.*, 1906, xvi, 358; 1908, xxi, 142; 1909, xxiii, 351;  
and *Archiv f. d. ges. Physiol.*, 1912, cxlvii, 111.
- <sup>7</sup> HIRSCHFELDER. "Diseases of the Heart and Aorta," Philad. and London, 1910, 107 and 108  
also *Bull. Johns Hopkins Hosp.*, 1907, xviii, 265, and 1908, xix, 319.
- <sup>8</sup> JOLLY AND RITCHIE. *Heart*, 1910-11, II, 205.
- <sup>9</sup> KREHL. *Abhandl. d. sächs. Gesellsch. d. Wissensch.*, 1891, xvii, 348.
- <sup>10</sup> ROTHBERGER. *Archiv f. d. ges. Physiol.*, 1907, cxviii, 353.
- <sup>11</sup> ROY AND ADAMI. *Practitioner*, 1890, xliv, 88-94.
- <sup>12</sup> STRAUB, H. *Journ. of Physiol.*, 1910, xl, 378-388; and also *Archiv f. d. ges. Physiol.*, 1911,  
cxliii, 83-87.
- <sup>13</sup> THAYER. *Boston med. and surg. Journ.*, 1908, clviii, 713, and *Archiv of internal Med.*  
1909, iv, 297.
- <sup>14</sup> WENCKEBACH. *Deutsch. Archiv f. klin. Med.*, 1911, ci, 411.



## ON THE SYSTOLIC BLOOD-PRESSURE IN THE ARM AND LEG IN AORTIC INCOMPETENCE.

By H. D. ROLLESTON.

(*St. George's Hospital, London*).

IN a paper on "The Measurement of the Systolic Blood-Pressure in Man," Hill (with the co-operation of Flack and Holtzmann<sup>2</sup>) in 1909 pointed out that in patients with aortic regurgitation there is a marked difference between the systolic blood-pressures in the arm and leg in the recumbent position, the systolic blood-pressure being higher in the leg than in the arm. This was explained as "due to the better conduction of the great systolic wave by the leg arteries, which were maintained in a somewhat contracted state in order to secure an adequate blood supply to the brain." In a later paper (1912) Hill and Rowlands<sup>3</sup> give numerous records of the blood-pressure in aortic regurgitation both uncomplicated and when combined with mitral disease. The maximum difference between the blood-pressures in the cases of aortic regurgitation given was 153 mm. Hg, the systolic pressure in the arm being 142 and in the posterior tibial 295 mm. Hg. It was also found that by immersing the legs in hot water the systolic pressure in the legs was reduced. Hill and Rowlands believe "that the hot water acts by inducing vasodilatation of the femoral arteries and so lessening the rigidity of the wall and the conductance of the systolic waves." Hare<sup>1</sup> confirmed these results and reported a case of aortic regurgitation in which the pressure in the arm was 275 and in the leg over 350 mm. Hg. This pathognomonic difference between the systolic pressures in the arm and leg also enabled him to establish the diagnosis of aortic incompetence in a case in which the ordinary physical signs were not sufficiently definite.

Since the publication of Hill's first paper I have found this difference between the systolic blood-pressures in the arm and leg in a large number of cases of aortic regurgitation. The difference varies considerably. In a young man aged 19, who was often under observation with very free but

compensated aortic regurgitation, the maximum systolic blood-pressure in the arm was usually about 140 mm. Hg, and that in the leg 350 mm. Hg, the difference of 210 mm. being remarkable. In another man aged 23 years with compensated aortic regurgitation there was a difference of 195 mm. (arm 125, leg 320).

In cases of aortic regurgitation, in which the compensation is strained or has broken down, the difference between the arm and leg pressures is less than in cases of compensated aortic regurgitation, but is usually distinct. I have seen cases in which, as in one of Hill's cases of combined aortic and mitral disease, there was less than 20 mm. Hg difference between the leg and arm pressures. In Hill and Rowlands' paper the records of the blood-pressure show very clearly that in uncomplicated aortic regurgitation the difference between the arm and leg pressures is considerably greater than in cases of combined aortic and mitral disease. Hill and Rowlands do not comment on this point, but their results render it unnecessary to give any further records.

In aortic regurgitation of recent origin, before compensation is established, the difference between the systolic blood-pressure in the arm and leg is comparatively slight or may even be absent. A boy aged 14 was admitted to St. George's Hospital in the third week of rheumatic fever with signs of pericarditis and aortic regurgitation. The systolic blood-pressure on different days were :—

| LEG. | ARM. |
|------|------|
| 120  | 100  |
| 90   | 100  |
| 100  | 90   |
| 130  | 120  |
| 95   | 95   |

A man with primary infective endocarditis of the aortic valves (confirmed by necropsy), which ran its course within 6 weeks, had a waterhammer pulse but the difference between the systolic blood-pressure in the leg (140) and in the arm (120) was only 20 mm. Hg.

It is natural to compare the effect of fever with that of the application of hot water to the legs on the systolic blood-pressure in aortic regurgitation. In a boy aged 17 years with aortic and mitral regurgitation and strained compensation the average difference between the systolic blood-pressure in the arm (130 mm. Hg) and the leg (185) was 55 mm. Hg; but during some attacks of fever, the highest temperature being 101·4 F., the difference



between the blood-pressures came down to 20 mm. and on one occasion even disappeared: the systolic blood-pressure fell greatly in the leg and only slightly in the arm. In a man aged 23 years with uncomplicated aortic regurgitation the average difference between the maximum systolic pressure in the arm (135 mm. Hg) and in the leg (200) was 65 mm. Hg. On one occasion he had slight fever (100.4) and the maximum systolic pressure in the arm was then found to be 145 mm. Hg. and in the leg 160: the difference was thus reduced to 15 mm. Hg by a fall in the blood-pressure in the leg.

Incidentally it is interesting to refer to a case of compensated aortic regurgitation with attacks of paroxysmal tachycardia in a man aged 23 years. When he was in his normal condition, some days before an attack of tachycardia, the systolic blood-pressures were 150 in the arm and 210 mm. in the leg: during an attack of tachycardia, in which the pulse rate reached 190 and neither the pulse or heart sounds suggested aortic regurgitation, the systolic blood-pressures on different days of the attack were 170 in the arm, and 180 in the leg; and 130 in the arm, and 150 in the leg, or differences of only 10 and 20 mm. Two days after the end of this attack, when the pulse rate was 72, the systolic pressures in the arm and leg were 130 and 170. On another occasion there was a difference of 90 mm. Hg some days before an attack of less severe tachycardia (pulse = 170), of 30 mm. during the attack, and an average of 60 for some days after the attack.

#### CONCLUSIONS.

(1) The difference between the maximum systolic blood-pressures in the arm and leg in aortic regurgitation is most marked in uncomplicated and compensated aortic regurgitation.

(2) It is much less marked in aortic regurgitation when the compensation is failing and, as Hill's records show, in cases of combined aortic regurgitation and mitral disease.

(3) In recent aortic regurgitation before compensation is established the difference is slight or may be absent.

(4) Fever, like the application of hot water to the legs diminishes the difference between the maximum systolic pressures in the arm and leg by producing a fall in the blood-pressure in the legs.

(5) In a case of aortic regurgitation the occurrence of paroxysmal tachycardia diminished the difference between the blood-pressures in the arm and leg.

## REFERENCES.

- <sup>1</sup> HARE. *Therap. Gazette*, 1910, 3rd ser. XXVI, 457.
- <sup>2</sup> HILL (with the co-operation of MARTIN FLACK and W. HOLTZMANN) *Heart*, 1909-10, I, 73.
- <sup>3</sup> HILL AND ROWLANDS. *Heart*, 1911-12, III, 219.



## OBSERVATIONS ON A CASE OF AURICULAR FIBRILLATION WITH SLOW VENTRICULAR ACTION.

By A. W. FALCONER AND GEORGE DEAN.

(Aberdeen).

A carriage cleaner, aged 55, was admitted into the Aberdeen Royal Infirmary on November the 18th, 1911, under Dr. Edmond, to whom we are indebted for permission to observe the case.

*Past history and habits.* The patient was quite healthy until he was about 35 years of age. He then had a severe attack of acute rheumatism with swelling of almost all his joints. He was in bed for over a month. About two years later he was again in bed for a fortnight with muscular rheumatism. About two years before admission to hospital he had another severe attack of acute rheumatism, which kept him in bed for some two months. About ten years before admission he acquired gonorrhœa, but there was no history of a chancre or of secondary symptoms of syphilis. For six years before admission he had suffered from breathlessness on exertion. This varied considerably from time to time, but for six years he had been practically unable to work. He had been a labourer all his life and had used alcohol and tobacco in moderation.

*Present affection.* Six weeks before admission the patient had an attack of "Influenza" and his breathlessness became considerably worse. On admission the patient was found to be a well developed man. He was able to lie in bed in any position without discomfort. There was no oedema. The apex beat of the heart was situated in the sixth interspace midway between the nipple and anterior axillary lines. On auscultation at the apex a loud systolic murmur, conducted well into the axilla, was heard. The second sound was sharp and was followed by an early diastolic murmur. Over the pulmonary area there was a systolic murmur and an accentuated second sound. The aortic sounds were pure. Over the tricuspid area there was a systolic murmur. The lungs appeared normal except for the presence of dry sounds at both bases. No enlargement of the liver was made out, and there was no evidence of ascites. The urine was moderate in amount and free from albumen. During his stay in hospital the patient remained, except for the last few days of life, in practically the same condition. He was quite comfortable as long as he was at rest, but he made no progress. His

temperature was at times a little irregular. On the 15th of February, 1912, he suddenly became much worse, having severe orthopnoea, and he rapidly developed physical signs of oedema in both lungs. He died on the 16th of February, 1912.

### *The polygraphic tracings.*

Numerous polygraphic tracings were taken throughout the patient's stay in hospital. They all showed the same characters. The pulse varied in rate from 38-56 beats a minute, but was generally between 40-48. During the last two days of life the pulse rose to 80, and the irregularity became more conspicuous, but tracings were not obtained on account of the dyspnoea. In none of the tracings was there a sign of a normal *a* wave. The great majority of radial beats occurred at regular intervals, but the rhythm, except on one occasion, was never perfectly regular. In short, the regularity was disturbed by the frequent occurrence of shorter cycles. These shorter cycles were quite irregular in their length and incidence. Fig. 1 is a tracing taken on the 20th of November, 1911. The first six beats are perfectly regular but the seventh beat is very definitely shorter. Fig. 2 was taken on the same date, half-an-hour after the subcutaneous administration of 1/25th gr. of atropine sulphate. The effect of the atropine on the pulse rate as counted at the wrist for a minute was inappreciable, but there was a very definite increase in the irregularity of the tracing. On November the 20th the patient was given ten minims of the tincture of digitalis three times a day and the dose was increased to 15 minims on the 22nd of November. On the 27th of November the pulse was, for the first time, perfectly regular over many yards of tracing, and the rate had fallen to 38. Next day, however, although the digitalis was continued as before the heart had reverted to the former slightly irregular rhythm. Occasionally a bigeminal action of the heart was present and on such occasions also, although the pause following the extrasystole was generally exactly equal to those following the beats of the regular ventricular rhythm, it was not invariably so. The extrasystoles did not always occur at exactly the same distances from the preceding ventricular contractions. Fig. 3 is an example of this rhythm taken on the 6th of December, 1911.

The case, therefore, was one of auricular fibrillation with a high degree of heart block which at times was probably complete.

### *Autopsy.*

The left pleural cavity contained 80 ounces of slightly blood stained fluid. The left lung weighed 15 ounces and was moderately emphysematous. The right pleural cavity was practically dry. The right lung weighed 32 ounces. The upper lobe was consolidated, deeply congested and oedematous. The lower lobes were moderately congested and showed distinct bronchiectasis.



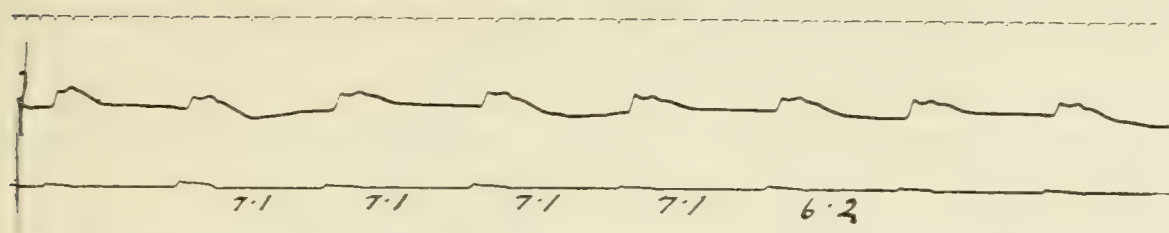


Fig. 1. Tracing taken on November the 20th, 1911. Ventricular venous pulse with slow irregular ventricular rhythm.

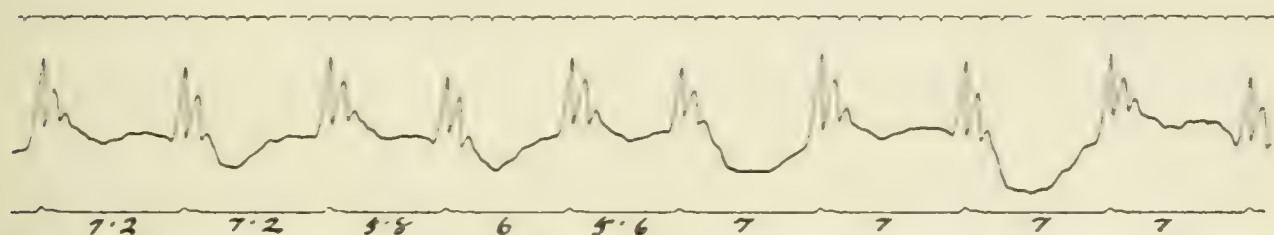


Fig. 2. Tracing taken on same date as Fig. 1, after one-twentyfifth gr. atropine sulphate. The irregularity is much more evident.

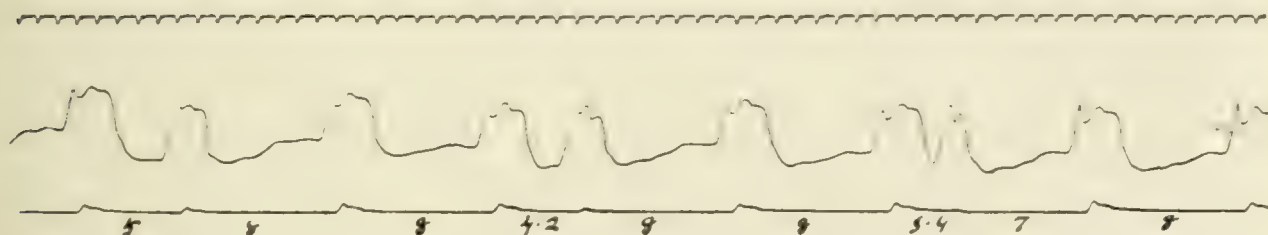


Fig. 3. Ventricular venous pulse with bigeminal action. (December the 6th, 1911.)

The bronchial glands were enlarged and indurated. The liver weighed 4 lbs. 8 ounces, and showed typical cyanotic atrophy. The spleen weighed 8 ounces and also presented the appearance of cyanotic atrophy. The right and left kidneys weighed respectively 8 and  $8\frac{3}{4}$  ounces. The capsules were slightly adherent and each kidney presented a few small cysts. The peritoneal cavity was dry.

*The heart.* In situ, the greatest longitudinal diameter was  $7\frac{1}{2}$  inches, the transverse  $5\frac{1}{2}$  inches. On removal of the heart, the pericardium was found to be densely adherent throughout with the exception of a small area

over the right auricle. The adhesion was almost entirely between the layers of the pericardium, but there was slight adhesion between the latter and the left costal pleura. A dense calcareous patch about an inch in diameter was situated in the pericardium and heart wall near the middle of the right ventricle. A similar patch was present in the posterior wall over the middle of the inter-ventricular septum.

The aortic cusps were conspicuously thickened, opaque, and rigid. There was no evidence of recent endocarditis. The wall of the aorta showed numerous atheromatous patches, many of them slightly elevated above the surface of the aortic wall. The orifices of the coronary arteries were considerably diminished and throughout their course the main coronary vessels were very thickened and calcareous.

The mitral valve presented the typical appearance of a button hole constriction, and only admitted the tip of the little finger. The cusps were thickened and rigid and the *chordæ tendineæ* were thickened and shortened. The cavity of the left ventricle, after hardening in formalin, measured  $4\frac{1}{4}$  inches, and the thickness of the wall was about one inch. The myocardium showed no great abnormality. The cavity of the right ventricle measured  $4\frac{1}{4}$  inches and the thickness of its wall varied from  $\frac{3}{4}$  to  $\frac{1}{2}$  an inch. The tricuspid leaflets were very thick and rigid and the orifice would not admit two fingers. The pulmonary cusps were slightly thickened, but were freely movable. The endocardium and myocardium of the right ventricle did not seem abnormal. The left auricle was dilated and the thickness of its wall was  $\frac{1}{4}$  of an inch. The right auricle was considerably dilated and its wall measured from  $\frac{1}{8}$  to  $\frac{3}{16}$  of an inch in thickness. The *tinea terminalis* was hypertrophied. The Eustachian valve was unusually well marked and distinctly thickened. It projected fully one inch into the cavity of the auricle. The coronary sinus was dilated and admitted the tip of the little finger. One and a-quarter inches from the orifice of the coronary sinus and just above the auriculoventricular junction, a rounded atheromatous patch  $\frac{9}{16}$  of an inch in diameter could be both seen and felt. On removing a block for microscopical examination this calcareous patch was found to be situated immediately above the anterior half of the membranous septum, and was not directly in the course of the *A-V* bundle. The membranous septum was thickened throughout, and was almost opaque to transmitted light.

For microscopical study blocks of tissue were taken from the following regions of the heart:—

1. The region of the sino-auricular node.
2. The *A-V* junction containing the *A-V* node and main stem of the *A-V* bundle. This block included the calcareous nodule already described.
3. Portions of the interventricular septum and of the left and right ventricles.



4. Portions of the left and right auricles.
5. Portions of the left and right musculi papillares.
6. The wall of the aorta.

1. *The sino-auricular node.* Serial sections 12 micra in thickness were cut through the sino-auricular node, and were stained with hæmotoxylin and eosin. The node was small and poorly developed, and was supplied by two arteries, the upper and smaller one evidently being a branch of the main vessel. Both arteries showed distinct thickening of their walls, but the lumina were not seriously reduced. Throughout the whole extent of the node, but more especially in the central portions, there was a profuse perivascular cellular infiltration. Just above the node and immediately below the pericardium, there was a typical submilliary nodule with giant cells characteristic of rheumatic infections. The wall of the vena cava also showed a profuse cellular infiltration extending throughout all its coats, and consisting of lymphocytes, plasma cells and multinucleated giant cells.

2. *The A-V junction.* As this block contained much calcareous matter it was decalcified in nitric acid for seven days and embedded in one block in paraffin. Serial sections were cut in 12-15 micra in thickness. From time to time, useful sections were only obtained with considerable difficulty owing to the presence of calcareous matter in the central fibrous body and for about a quarter of an inch in this region we were unable to obtain useful sections.

Throughout the whole course of the A-V node and main stem of the bundle there were extensive pathological changes. These varied both in character and extent in different parts of the system.

The A-V node and first part of the bundle were densely fibrosed and to a large extent replaced by fully formed fibrous tissue. In places the destruction was complete except for a thin flattened band of muscular tissue at the periphery of the bundle. Here and there throughout the fibrous tissue there were dense foci of cellular infiltration. These foci consisted of small round cells, the majority of which were lymphocytes and plasma cells. There were also a few fibroblasts and endothelial like cells. The artery to the bundle showed considerable thickening of its coats. Fig. 4 and 5 are from the A-V node and the upper part of the main stem. Passing downwards towards the ventricles the muscle tissue of the bundle was better preserved, but throughout was more or less fibrosed, and in parts densely infiltrated with cells. The central fibrous body contained large calcareous deposits in the immediate neighbourhood of the bundle, and it was freely infiltrated with cells similar to those described in the bundle.

Throughout its course in the membranous septum the bundle was more or less fibrosed and its outline deformed. In some places apparently quite a third of the muscular tissue was replaced by fully formed fibrous tissue which intersected the bundle in all directions, and which in successive sections could be seen destroying and replacing comparatively large portions of the muscular tissue of the bundle. The membranous septum showed considerable cellular infiltration, and a number of the vessels were completely thrombosed. The calcareous nodule, seen macroscopically above the anterior half of the membranous septum, consisted of a dense mass of fibrous tissue containing the remains of the calcareous material, which had resisted decalcification. The nodule, however, did not involve the bundle. Fig. 6 and 7 are from the membranous septum.

3. *Portions of the interventricular septum and of the right and left ventricles.* Throughout the interventricular septum there was a meshwork of connective tissue which was for the most part fully formed. A few foci of fibroblasts were present here and there. Enclosed within the connective tissue were numerous muscular fibres in various stages of atrophy. The arteries showed considerable thickening of their coats. Both right and left ventricles presented similar changes to the above, but to a less extent. There was a patchy fibrous thickening of the endocardium in both chambers. There was some cloudy swelling, but no fatty degeneration. The nuclei of the muscle cells were considerably altered and showed karyorrhexis and karyolysis, but it is probable that most of these nuclear changes were of post mortem origin.

4. *Portions of the right and left auricles.* Both auricles, but more especially the left, showed a considerable degree of chronic myocarditis similar to that seen in the interventricular septum. There was a patchy thickening of the endocardium in both chambers. There was no fatty degeneration.

5. *The muscoli papillares.* There was a well marked fibrosis of the muscoli papillares. The walls of the arteries were greatly thickened, both the intima and media being affected. There was no fatty degeneration.

6. *The aorta.* There was wide-spread fatty degeneration of the endothelium and the sub-endothelial connective tissue. The pale yellow plaques described in the naked eye description consisted of cells which were all in a state of advanced fatty degeneration. In the walls and in the perivascular lymph spaces of the vasa vasorum in the outer coat of the aorta, was an extensive infiltration consisting chiefly of lymphocytes but with a few endothelial cells.

Autopsies in cases of auricular fibrillation with slow ventricular action have been recorded by Esmein,<sup>3</sup> Draper,<sup>2</sup> Cohn,<sup>1</sup> Price and Ivy Mackenzie,<sup>7</sup> and the present writers.<sup>4</sup>



Esmein reports two cases in both of which old lesions of the *A-V* bundle were present, but we have been unable to obtain the original publication. Cohn has reported the anatomical findings in one of Mackenzie's cases<sup>6</sup> (*CASE 3*). In this case the block was clinically incomplete.\* Cohn found "profound lesions of the sino-auricular node, interstitial myocardial lesions in the auricles and ventricles, but more especially in the right auricle, with but slight changes in the auriculo-ventricular node and branches."

Draper's case was also clinically one of incomplete block. He discovered throughout the whole length of the *A-V* node and main stem, patches of fibrous tissue with here and there collections of small round cells, but he states that despite the presence of the fibrous patches and the small round cell infiltration there seemed still to be a large amount of muscle fibre present.

Price and Ivy Mackenzie have described a case under the title of auricular fibrillation and heart block. The only evidence however of auricular fibrillation and heart block consists in a somewhat unsatisfactory tracing, the interpretation of which, as the authors themselves point out, is not absolutely clear. The cardiac condition followed diphtheria. At the autopsy they discovered extreme degeneration and cellular infiltration of the cardiac muscle, especially in the ventricles and mainly distributed in the course of the vessels. Beyond a vacuolated appearance of the fibres of the auriculo-ventricular node there was no change in the node or bundle. Freund<sup>5</sup> has described the post mortem findings in three cases of auricular fibrillation with incomplete heart-block. In two of the cases the pulse rate varied between 60 and 70 a minute. In both he discovered marked fibrosis of the bundle of His with here and there acute small celled infiltrations. The third case presented an irregular pulse of about 45 a minute and the autopsy disclosed almost complete destruction of the auriculo-ventricular node and *A-V* bundle, by extremely dense fibrous tissue, with here and there a profuse small celled infiltration.

In the present writers' previous case, which was clinically one of complete block, there was complete destruction of a considerable portion of the main stem of the *A-V* bundle with obliteration of the artery to the bundle.

#### SUMMARY.

A case of auricular fibrillation with incomplete heart-block is reported. Post mortem in addition to various valvular and muscular lesions there was extensive fibrous and cellular infiltration of the *A-V* node and bundle. There was also cellular infiltration of the sino-auricular node.

---

\* That is to say, the action of the ventricle was irregular.

## BIBLIOGRAPHY.

- <sup>1</sup> COHN. Heart, 1911-12, III, 23.
- <sup>2</sup> DRAPER. Heart, 1911-12, III, 13.
- <sup>3</sup> ESMEIN. Revue mens. d. méd. int. et de thérap., 1909, 1-609. Quoted from Archiv. d. Malad. d. Cœur, 1910, 256.
- <sup>4</sup> FALCONER AND DEAN. Heart, 1911-12, III, 247.
- <sup>5</sup> FREUND. Deutsch. Archiv. f. klin. Med., 1912, CVI, 1.
- <sup>6</sup> MACKENZIE. Heart, 1909-10, I, 23.
- <sup>7</sup> PRICE AND IVY MACKENZIE. Heart, 1911-12 III, 233.



4. Corn  
bundle.  
of the pli

5. Sect  
Dense co  
infiltrates  
in the pli

6. Sect  
a consid

7. Secti

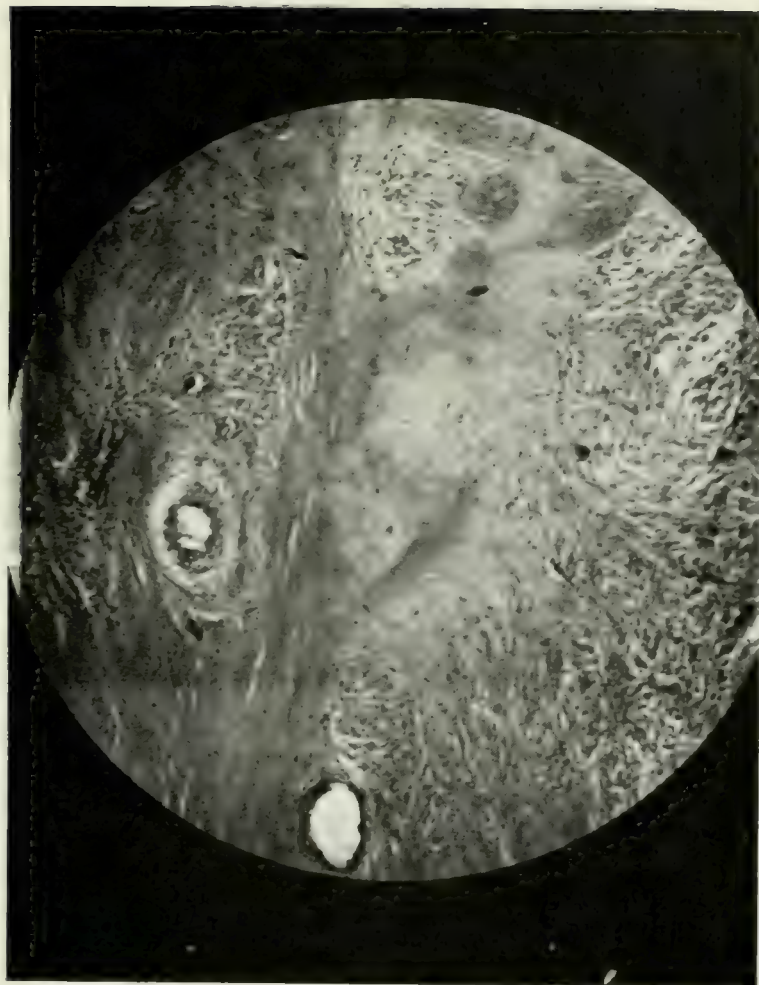


Fig. 6.

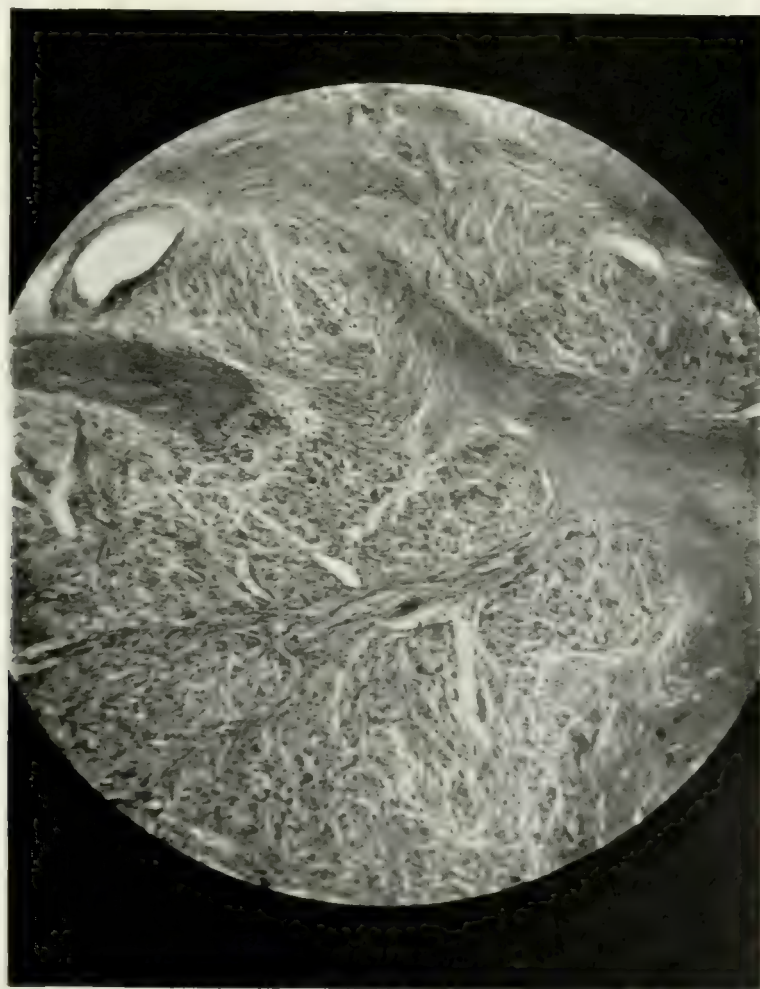
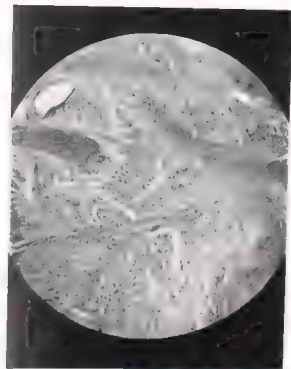
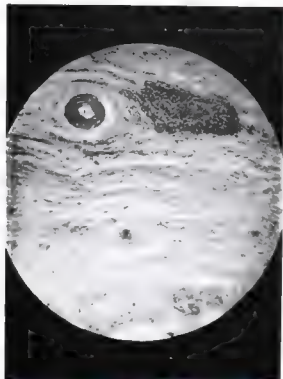
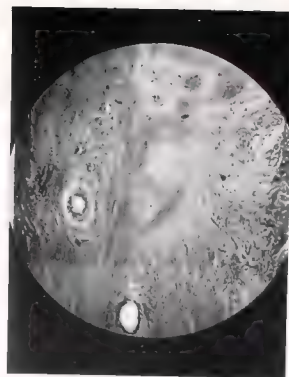
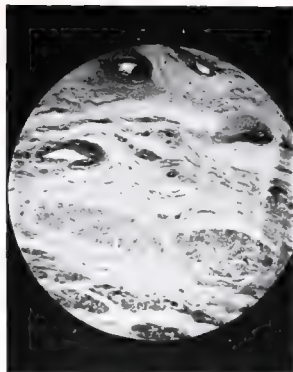


Fig. 7.





## RHYTHMIC CHANGES IN THE HUMAN HEART-BEAT.

BY G. CANBY ROBINSON AND GEORGE DRAPER.

(*From the Hospital of the Rockefeller Institute for Medical Research, New York*).

### INTRODUCTION.

THE following paper discusses three cases in which the mechanism of the heart-beat changed in a rhythmic manner. These changes have been recorded by means of electrocardiograms and venous tracings, and so analyzed. In the curves from all of the cases, groups of beats are seen which the electrocardiograms and the venous tracings indicate are abnormal. These abnormal groups alternate rhythmically with heart-beats of apparently normal origin and course. They recur at regular intervals and the groups show a striking similarity to one another in each case. As the type of abnormal beat is different in each case, a separate description and discussion of each will be given and then the points common to all will be considered.

### PART I. (CASE 1.)

*History.* The patient is a well developed boy of seventeen years, apparently in perfect health. His childhood is said to have been free from severe illness and the history contains nothing which may be considered as an etiological factor in the production of a cardiac disorder. In 1905, at the age of eleven, it was accidentally discovered that his heart was irregular. He was given strophanthus, digitalis and other drugs for about two years without apparent effect on his arrhythmia. His exercise, which had been sometimes quite violent previous to the discovery of the arrhythmia, was somewhat restricted. Except for palpitation, which occurred occasionally when his attention was directed to his heart, he has always been free from cardiac symptoms, even during active exercise. Since the arrhythmia was first noted six years ago, the pulse has been usually irregular or abnormally rapid. At times, however, a regular normal rate has been noted for short intervals, especially during mental excitement. The numerous forms of cardiac action that have been observed will be demonstrated by the curves.

*Physical examination.* Physical examination, except for the irregular or rapid heart action, is negative. The heart is perhaps slightly enlarged, compared to the size of the chest, the apex beat being felt in the fifth space

9.5 cm. from the mid-line. Cardiac dullness extends 3.75 cm. to the right and 10.25 cm. to the left. No cardiac murmurs are heard, but an indefinite gallop rhythm at the apex is noted at times. The systolic blood pressure is 93, the diastolic 75 mm. Hg.. The heart beats regularly at 121 per minute. X-ray plates and fluoroscopic examination show evidence of enlarged mediastinal glands, but no other abnormalities.

*Description of curves.* The curves have been taken at various times between March the 21st, 1910, and April the 23rd, 1911, during which time the large number of observations showed that the cardiac condition remained practically unchanged.

Fig. 1, taken with the slow speed of the Jacquet sphygmocardiograph, shows the arrhythmia which was most commonly observed. The tracing from the radial artery shows that the arrhythmia consists of short alternative periods of rapid regular beats and slower coupled beats. The most striking feature of the curve is the exact correspondence between analogous parts of the various groups. Each of the three groups begins with three moderately shortened waves, the last of the three being the longest. These waves are then followed by a group in which the rate is about 125 per minute, and each group terminates with a prolonged wave. This peculiar rhythmic change in the pulse was observed many times over a period of months. It represents the usual cardiac activity in this case and varies only slightly in the number of beats which constitute the rapid or slow groups.

Fig. 2 and 3, arterial and venous tracings, taken on a more rapidly moving recording surface, demonstrate further details of this peculiar rhythm. In Fig. 2, obtained on the same day as Fig. 1, the ending of one and the beginning of the next rapid group are seen. Between these groups there occurs but one normal cardiac cycle of 0.84 seconds in duration in the arterial tracing, accompanied by the three normal *a*, *c* and *v* waves in the venous tracing. This normal heart-beat always precedes a group of rapid beats, and for purposes of identification, it is marked (X) in all the curves in which it is seen. This beat represents the first of the three moderately shortened waves which are seen in Fig. 1 to usher in a group of rapid beats. In Fig. 2 the venous tracing shows that in the next beat a small abnormal wave follows the *c* wave, marked *a*<sup>1</sup>, falling between it and the *v* wave. During the remainder of the tracing this abnormal wave becomes more prominent and the *c* wave is no longer preceded by a normal *a* wave.

The two following beats in all the many groups recorded, the second and third beats after the normal one, have always constant characteristic features in the venous tracings. In the first of the two beats the wave following the *c* wave, marked *a*<sup>1</sup>, becomes prominent and is distinct from the *c* wave, but is more or less fused with the *v* wave. In the following beat, the *c*, *a*<sup>1</sup> and *v* waves are usually partly fused, forming a large rounded or notched wave. The radial tracing accompanying these three characteristic waves in the venous tracing has also constant features. The first pulsation is



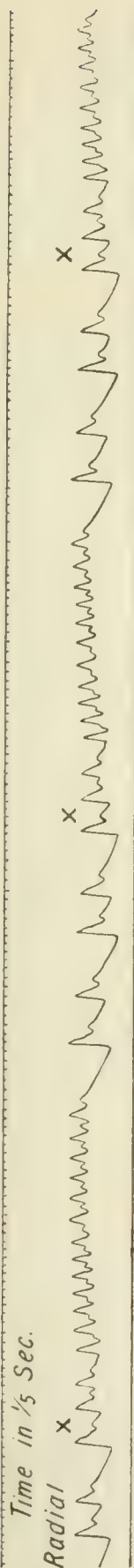


Fig. 1. (Redrawn.) *CASE 1.* Tracing from radial artery taken with the slow speed of the Jaquet sphygmocardiograph, showing the arrhythmia which was most commonly observed.

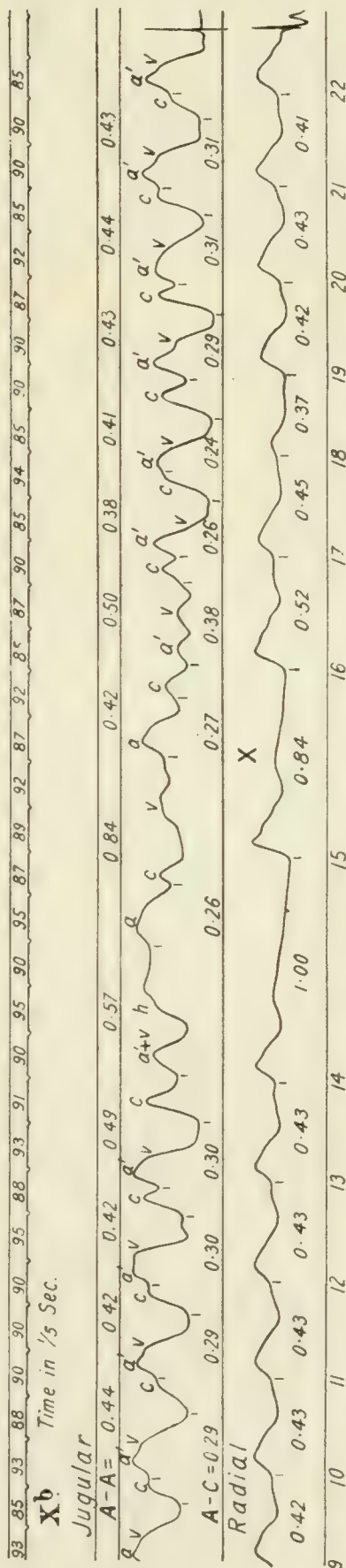


Fig. 2. (Redrawn.) *CASE 1.* Arterial and venous tracings taken on a rapidly moving recording surface, demonstrating further details of this peculiar rhythm. All measurements are in seconds. Time marked in one-fifth seconds in all curves. (March the 31st, 1910).

always about 0.50 seconds in duration, the second somewhat shorter, provided there is any wave in the radial tracing accompanying the partly fused rounded or notched venous wave. The arterial pulse of this beat is often too weak to produce a wave in the tracing, and at best causes only a very small wave of short duration.

Following these three distinctive cardiac cycles, the remainder of the group of rapid beats show in the venous tracing large *c* waves followed by an even larger wave, marked  $a^1$ , falling between the *c* and *v* waves, partly fusing with the latter.

Fig. 3, obtained more than a year later, shows two groups of rapid beats which are in all essentials like those seen in Fig. 2. The two groups in Fig. 3 show a remarkable similarity to each other, especially when the details of the venous tracings are compared, and indicate how truly rhythmic these changes in the heart-beat are. Between groups I and II of this figure there are several slow beats which have not been reproduced. Here it is again seen that each group consists of the normal beat (marked X), the three characteristic cycles which have been described and a series of four more rapid beats. Here the third cycle of the group produces the usual fused notched wave in the venous tracing, but fails to produce a definite wave in the arterial tracing.

Fig. 4 is an electrocardiographic record which shows a group of rapid beats. The normal electric complex with the usual positive *P*, *R* and *T* waves is seen only in the cardiac cycle number 2 (marked X). In all the others there is distortion in the curve, indicating some cardiac activity just before the onset of the *T* wave, with which an abnormal wave is partly fused. Complexes 3, 4 and 5 represent the three cardiac cycles which always cause characteristic effects in venous tracings, and except for the variations in the relation which the abnormal wave, marked  $P^1$ , bears to the following *R* wave, they do not seem to differ from the other complexes forming the group. This relation of  $P^1$  and *R* will be discussed later. In passing, it is worthy of note that although the third heart-beat of the group never produces as strong an arterial pulse as the others, nothing to differentiate it from the other beats is seen in the size or shape of the *R* wave.

In Fig. 5 the venous tracing is recorded synchronously with the electrocardiogram, and the relation of one to the other is shown. Two pairs of coupled beats are seen, the first of each pair being a normal beat, showing the usual waves both in the electrocardiogram and in the venous tracing. In the second beat of each couple, the *T* wave in the electrocardiogram is deformed just as are all the *T* waves which occur in the latter part of the curve where a group of rapid beats begins. In these parts of the venous tracing which correspond to the same portions of the cardiac cycle, there is an abnormal wave or distortion, marked  $a^1$ , scarcely noticeable in the first part of the curve, but quite prominent in the latter part.



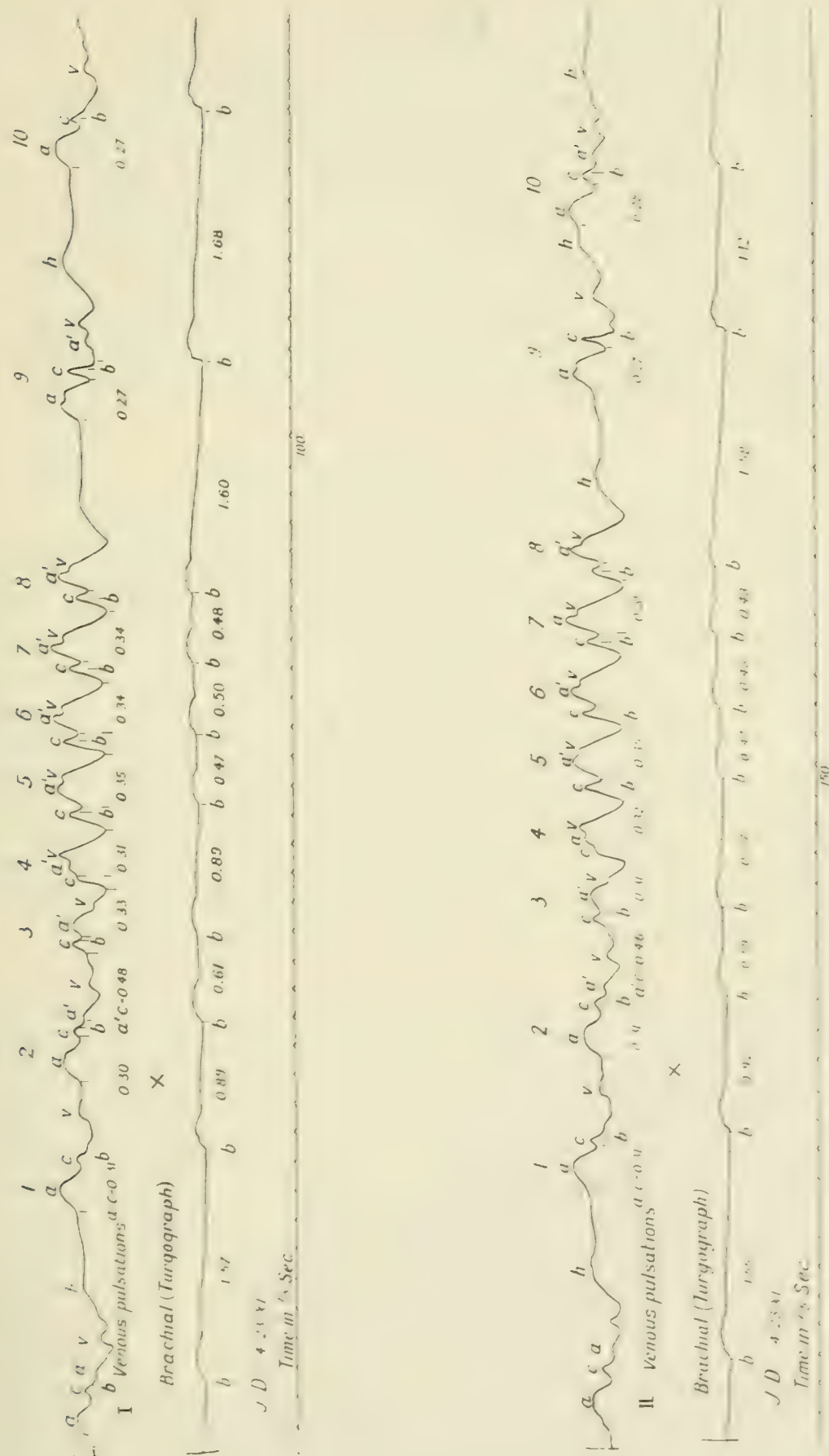


Fig. 3. (Redrawn.) *CASE 1.* Arterial and venous tracings showing two consecutive groups of rapid beats. (April the 23rd, 1911).

*Discussion of CASE I.*

The cardiac activity which causes these unusual forms of electrocardiographic and venous tracings allows but one interpretation. It is evident that an auricular contraction occurs during ventricular systole, sending a wave into the veins of the neck between the *c* and *v* waves, and moving the string of the galvanometer between the *R* and *T* waves. The fact that this wave in the electrocardiogram, marked *P*<sup>1</sup>, differs conspicuously in form from the normal *P* wave in this case may be taken as evidence that the auricular activity which gives rise to it is ectopic; that is, it originates outside of the usual region of stimulus formation. It will be spoken of, therefore, as the auricular extrasystole. Other examples, recorded by the string galvanometer, of very similar auricular extrasystoles have been published by Lewis<sup>10</sup> and by Rosenthal.<sup>16</sup>

*Effects of the auricular extrasystole.*

The most satisfactory interpretation of the various rhythms which this case presents is based on the variety of effects which the auricular extrasystole produces upon the cardiac action. The effect produced depends on whether the auricular extrasystole stimulates ventricular contraction or whether it is blocked.

(a) *Blocked extrasystoles.* During the periods of slow cardiac action, the extrasystole never stimulates the ventricles to contract. It may occur during each ventricular systole, as is seen in Fig. 6, when the pulse is very slow and regular. More often, however, every other ventricular systole is accompanied by a blocked auricular systole, as in Fig. 5, and then the slow coupled rhythm takes place. The coupled rhythm is caused by the prolongation of the diastoles following the auricular extrasystoles.

(b) *Effect of the extrasystoles when they are not blocked.* (1) *Rhythmic success and failure of extrasystoles to control the movements of the ventricles.* The fact that the auricular extrasystoles may suddenly cease to be blocked and temporarily control the movements of the ventricles is the essential phenomenon in the mechanism of the production of the groups of rapid beats. It is seen in all the curves that show these groups (especially well in Fig. 4) that after a normal cardiac cycle, the group is always inaugurated by an auricular extrasystole which, after an abnormal delay in conduction, stimulates a ventricular systole. There is no evidence of normal auricular activity between this auricular extrasystole and the next ventricular contraction. After the extrasystole once succeeds in stimulating the ventricles to contract, the stimulus seems to pass more readily from the auricles to ventricles, and the conduction time of the second beat of a group is always much shorter than that of the first. Thus in Fig. 5 the conduction time of the first beat of the group is 0.41 sec., and of the second beat 0.25 sec..



This improvement in conduction is only temporary and the time between auricular and ventricular activity gradually lengthens, beat by beat, until the extrasystole fails again to excite ventricular contractions. The slow rhythm is then re-established, the ventricular systoles being preceded by normal auricular contractions, and continues for several beats until the abnormal pace-maker again establishes itself. An exact repetition of the previous group, as seen in Fig. 3, then takes place. It is this alternating success and failure of the auricular extrasystoles to stimulate ventricular contractions that produces the rhythmic changes in the heart-beat.

(2) *The dominance of an extrasystolic rhythm over prolonged periods.* The auricular extrasystole may, after becoming established as the pace-maker for the ventricles, retain this function over relatively long periods of time. The persistence of the rapid rate is seen in Fig. 7, where it follows suddenly upon a long stretch of coupled beats. The behaviour of the pulse at the time of this change is the same as that which occurs at the onset of a small group of rapid beats. In Fig. 8, synchronous venous pulse tracing and electrocardiogram also show the heart beating at a persistently rapid pace, as in the latter part of Fig. 7. It is seen that the *T* wave of the electrocardiogram is deformed in each cycle by an unusually sharp upstroke, that in the venous tracing there is a large wave between the *c* and *v* waves, and that there is no other evidence of auricular activity. These waves make it certain that an auricular contraction occurs during each ventricular systole, and stimulates the next ventricular systole after a long conduction time. It is clear then that the auricular extrasystole may retain the function of the pace-maker of the heart over a relatively long period of time, and produce a rapid and regular heart action.

#### *The action of the cardiac nerves.*

(a) *Effect of psychic excitement.* A number of observations were made which seem to indicate a distinctly abnormal nervous control of the heart in this case. It was found that under psychic excitement, the heart could beat with a practically normal rhythm, entirely undisturbed by auricular extrasystoles. In April, 1910, the patient was brought from Philadelphia to New York in order to obtain electrocardiograms, through the kindness of Dr. Walter B. James. It was noticed during the journey that the arrhythmia had disappeared and the heart was beating practically regularly at about 80 per minute. The pulse continued to be regular during the journey and after arriving at the Presbyterian Hospital, where exercise, rest, ice to the præcordium and other measures failed to disturb the normal rhythm. At this time the curve shown in Fig. 9 was obtained. The electrocardiogram is quite normal as regards the form of the various waves, although the conduction time is abnormally long. It measures 0.20 to 0.21 sec., but is shorter in this curve than in those obtained during the usual

abnormal rhythm. This curve shows a definite irregularity in the lengths of the individual cycles, a conspicuous sinus arrhythmia being present.

The heart continued to beat in a practically normal manner for three days. The usual arrhythmia appeared only once during this time, and then for a short period only, after the patient had been resting quietly for some time, but the heart resumed the normal rhythm before records could be obtained. Finally, on the morning of the fourth day, a persistent arrhythmia established itself and records of groups of rapid beats resembling those in Fig. 4 were made. During the years of observation, this has been the sole occasion upon which persistent normal action has been recorded.

(b) *The effect of ice upon the præcordium.* On several occasions it was noticed that the cardiac rhythm could be changed by applying ice to the præcordium, the patient being quiet in the recumbent position. This effect was obtained only when the heart was beating at an abnormally rapid rate, as in Fig. 8. The change usually took place in from five to fifteen minutes, and either the usual group rhythm or a slow regular pulse resulted. On one occasion the heart rate was 123 per minute and regular before the application of ice. About five minutes afterward, the rate had fallen to 42 per minute (Fig. 6). Deep inspiration seemed sometimes also to change the rapid rhythm into a slow regular or coupled rhythm, or into the grouped rhythm.

(c) *The effect of vagus pressure and atropine.* Pressure over neither the right nor the left vagus nerve produced any change in the cardiac rhythm, and from this fact it was considered that the vagus tone was low. In order to test this question further, the patient, who was at the time under observation in the Hospital of the Rockefeller Institute, was taken to the electrocardiographic room and a series of records were made. Atropine sulphate (0.6 mg.) was injected hypodermically and about fifteen minutes later the changes in the rhythm, which had been obtainable by very deep forced inspiration, were no longer elicited. The heart increased in rate in a startling manner and beat perfectly regularly at 180 per minute. At this time the patient developed cardiac sensations, which he had never had before and which caused him considerable anxiety. He said he felt as though the heart were trying to leap out of the chest. The cardiac contractions were very violent and shook the whole thorax. A striking feature of the condition at that time was the reference of all symptoms to the violent heart action. There was neither dyspnœa nor any change in colour. All the ventricular beats produced radial pulsations; these, however, were small and soft. In about two hours slight slowing followed deep inspiration, and in about two and a-half hours after the administration of the drug, this effect of deep inspiration was conspicuous. The heart action quieted down after this interval. Later in the day the patient felt quite well and showed no objective signs of cardiac inadequacy. Fig. 10 was obtained while the patient was under the effect of atropine; the rate was 164 per minute.



The experience with atropine throws much light on the nervous control of the heart in this case. It is well known that atropine removes the heart from vagus control by producing a paralysis of the inhibitory nerve endings, and there seems to be no doubt that it was through the removal of the vagus inhibition that the very rapid heart action resulted. As the paralysis of the vagus action caused so great an increase in rate, it must be concluded that the vagus tone was constantly high and that its inhibitory power controlled a heart which would otherwise have beat at an abnormally rapid rate.

The fact that the patient had marked cardiac sensations only during the height of the rapid rate after atropine suggests the possibility that at this time the heart-beat passed the so-called critical rate described by Wenckebach.<sup>21</sup> Symptoms which may arise and disappear suddenly with changes of rate during attacks of paroxysmal tachycardia, have been ascribed with good reason by Wenckebach to what he calls auricular plugging ("Pfropfung"). The symptoms apparently arise when the auricles, contracting during the ventricular systole of the preceding cardiac cycle, are unable to propel the blood forward into the ventricles. He points out the role which delay in conduction may play in producing the coincidence of auricular and ventricular systole and shows how it interferes with the pumping mechanism of the heart. Fig. 10 shows this coincidence of auricular and ventricular contraction, for the *P* wave is seen to lie between the *R* and *T* waves. The mechanism which Wenckebach has described is therefore present here, and might account for the symptoms which were observed. In Fig. 8, however, both the electrocardiogram and the venous tracing show the same coincidence of auricular and ventricular systoles that is seen in Fig. 10. Although there is a considerable difference in rate, this auriculo-ventricular relation is maintained by the lengthened conduction time. It appears then that the mechanical conditions were quite suitable in both instances (Fig. 8 and 10) for the production of symptoms. But since none were present when the curve in Fig. 8 was obtained, some doubt is attached to the mere coincidence of the auricular and ventricular systole as the sole factor in the production of symptoms after the heart has passed the so-called critical rate in paroxysmal tachycardia.

#### *The production of the auricular extrasystole.*

The auricular extrasystole presents some features which must be considered with the hope of gaining a clearer insight into the various phenomena of this case. It is a striking fact that the extrasystole never occurs except when preceded by a ventricular systole. Both the electrocardiograms and the graphic records show that under all conditions the onset of the auricular extrasystole occurs at a constant length of time after the onset of ventricular systole. This time is so short that the extrasystole begins before the end of ventricular systole, always accompanying rather than following the ventricular activity. The extrasystoles in the curves of Lewis

and of Rosenthal, mentioned above, also showed a constant relation between their onset and that of the preceding ventricular systoles. This constant relation suggests that the ventricular activity in some way determines the onset of the auricular extrasystole, or that both are determined by the same factor. If curves such as those in Fig. 8 and 10, when a constantly rapid rate is maintained, were studied alone, the conclusion might seem justified that some point in or near the atrio-ventricular system had assumed the function of the cardiac pace-maker. But when the other curves are considered, this assumption is very improbable. When the rate is slow these extrasystoles occur during ventricular contractions which are obviously inaugurated by the preceding normal auricular systoles. It is unnecessary, therefore, to consider that the junctional tissues are the site of common stimulus production for the sequential ventricular systoles, and for the auricular extrasystoles. The point of origin of the extrasystoles must be left undetermined. When the rate is rapid, the time relations between the onset of the auricular extrasystoles and of the ventricular systoles are such that it seems impossible that both auricles and ventricles could be stimulated from some abnormal point lying between them. The  $P$ - $Q$  time (Fig. 10) is 0.18 to 0.20 sec., while the  $Q$ - $P$  time is about the same. If some point in the junctional tissues stimulated both parts of the heart simultaneously, these points, indicating the onset of auricular and ventricular contractions, would fall nearer together. The mechanism of the heart-beat when the rate is rapid is therefore not dependent on atrio-ventricular stimuli. The origin of the extrasystoles, both when it is followed by ventricular systoles and also when it is blocked, lies probably above the junctional tissues. The significance of the constant relationship between the onset of ventricular contractions and of the auricular extrasystoles is not clear.

*The rôle of the cardiac nerves in determining the variations in rhythm.*

This case presents a variety of rhythms which change from one to another readily and suddenly. Psychic excitement, ice to the præcordium, rest and the administration of atropine are factors which all influence the cardiac rhythm. It is evident, therefore, that extracardiac influences can change the rhythm, and that these influences are apparently active through the nervous mechanism controlling the heart. Besides the variations in the effect which the auricular extrasystoles have on the ventricular rate, there are also variations in the occurrence of the extrasystoles, as at times they occur with every ventricular systole, at times with every alternate systole and during one period they failed to occur.

There is comparatively little experimental evidence for the belief that such abnormal cardiac rhythms are produced through the action of the cardiac nerves. It is well known that the so-called cardiac properties of rhythmicity, conductivity, irritability and contractility are under the influence of the vagi, which nerves are in a state of constant tone. Hunt<sup>5</sup>



has shown that the cardiac accelerators are also in tonic activity and that the most important functions of the accelerators seem to be connected with their constant state of tone. Hunt's work and that of Rothberger and Winterberg<sup>17, 18 & 19</sup> lead to the conception that the cardiac functions stand between a constantly balanced nervous mechanism, the vagi opposing the accelerators. The state of the various cardiac properties at any one time will depend then on the relative predominance of the vagus influence over the accelerators, or *vice versa*. Hunt's experiments led him to conclude that change in vagus tone was the most important factor in the production of changes in the heart-beat in the normal mammal.

In the case under discussion there is at least one fact which demonstrates that the nervous control of the heart was abnormal and suggests that nervous influences were largely responsible for the variations that were seen. When atropine was given, the heart action was very rapid and the conduction time was reduced to within the normal limit. At this time it can be safely asserted that the action of the accelerator nerves predominated over the action of the paralysed vagi. By analogy it seems very probable that the tone of the vagi was reduced when a constantly rapid rhythm, as seen in Fig. 8, was in progress. It seems probable also that the changes from this type of rapid rate to slower rates when the auricular extrasystoles became blocked, resulted from an increase of vagus tone relative to that of the accelerators. The rhythmic changes of the heart-beat may be explained, therefore, by rhythmic variations in the nervous control of the heart. When the accelerator tone was relatively high, the extrasystoles accompanied all ventricular systoles and were always able to stimulate ventricular contractions. When the vagus tone was relatively high the extrasystoles occurred with alternate ventricular systoles only, and were always blocked. During the times when these two conditions alternated, causing the characteristic rhythmic changes, it may be assumed that the tone of the vagi was periodically increased and diminished relatively to that of the accelerators. During the period of several days when the auricular extrasystoles were absent and the heart action was relatively normal, the condition of the heart seemed to be farther removed from its condition after atropine than at any other time. It would seem likely, therefore, that at that time the highest degree of vagus tone was present and that psychic excitement was the cause of raising the vagus tone.

Although periodic changes in the tone of the cardiac nervous mechanism may account for the rhythmic changes in the heart-beat, the fact that the changes occurred so often each time after the same number of beats suggests that rest and fatigue of the heart muscle may itself play a part in the determination of the rhythmicity. The heart muscle, however, would be held by the cardiac nerves in such a state that neither the rapid nor the slow rate could be permanently maintained, so that they probably do play a part at all times in determining the cardiac action, although under certain conditions rhythmic rest and fatigue of the muscle itself may come in as a causative factor.

*Summary.*

A variety of disturbances of cardiac rhythm have been described in an otherwise healthy boy. The usual type of disturbance in this case was one in which the rate altered in a rhythmic manner, producing small groups of rapid beats between which slow and regular or coupled beats occur. Either the rapid rate of the groups or the slow rate occurring between them might persist over a relatively long period of time. These various changes in the cardiac rhythm were the result of the effects which auricular extrasystoles have on the heart-beat. Different effects were produced, according as the extrasystoles stimulated ventricular contractions or were blocked. The alternate success or failure of the auricular extrasystole in stimulating the ventricles caused the rhythmic changes in the heart-beat.

The auricular extrasystoles bore in all types of rhythm, a constant relation to the preceding ventricular systole. The significance of such a constant relationship is not clear.

The nervous control of the heart was distinctly abnormal and the cardiac rhythm was very susceptible to various agents which influenced the cardiac nervous mechanism. Psychic excitement was accompanied by a normal heart-beat, and this was seen under no other conditions; atropine caused a rapid tachycardia. The changes in the cardiac rhythm were apparently the result of changes in the nervous control of the heart, although the frequent and rhythmic variations may have depended in part on alternating states of rest and fatigue of the heart muscle itself.

## PART II. (CASE 2.)

*History and physical examination.* The second case of rhythmic changes in the heart-beat occurred in a girl of seven, who suffered from mitral insufficiency, apparently of rheumatic origin, and probably from myocardial insufficiency. She was admitted to the Hospital of the Rockefeller Institute on April the 18th, 1911, in a state of fair compensation. Besides tonsillitis before the age of five and diphtheria at that age, the patient had an attack of acute articular rheumatism two months before admission. Her cardiac symptoms, consisting largely of dyspnoea, usually had occurred only after exercise. On several occasions definite breaks in compensation followed violent exertion. On admission the physical examination was practically negative except that the heart was enlarged. The area of cardiac dulness extended 4.25 cm. to the right and 12.5 cm. to the left. There was a systolic murmur of mitral insufficiency at the apex and the heart was beating forcibly 110 times per minute.

Digitalis was administered (0.5 cc. of the tincture every four hours) from April the 29th until May the 7th. On April the 30th it was first noticed that an irregularity simulating a sinus arrhythmia was present, and it seemed



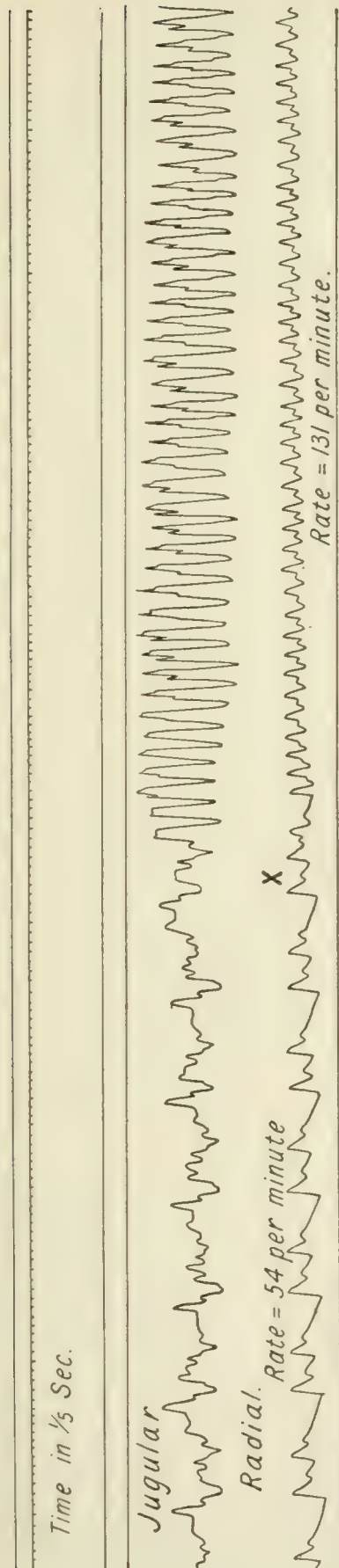


Fig. 7.—(Redrawn.) CASE 1. Arterial and venous tracings showing a relatively persistent bigeminal pulse, changing into a relatively persistent rapid pulse.

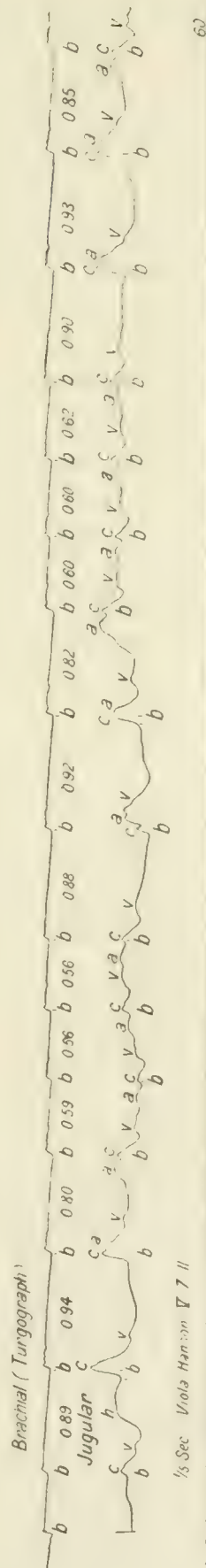


Fig. 11. (Redrawn.) CASE 2. Arterial and venous tracings showing three groups of slow beats, alternating with rapid beats. Measurements are in seconds.

even more noticeable on the following day. The arrhythmia persisted and on May the 8th it consisted of a series of fairly rapid beats, then two slower cycles, and then another series of rapid ones. Conspicuous slowing followed deep inspiration. On the next day it consisted of two, or occasionally three slow irregular cycles, followed by four, five or six more rapid ones. Deep inspiration caused a considerable increase in the number of slow irregular beats. The patient left the hospital on this day in good condition and returned for observation three days later, when the heart was beating regularly. The arrhythmia was not present when the patient was seen again in August, 1911.

*Description of the curves.* Records of the arrhythmia were obtained in synchronous tracings from the venous and brachial pulse and in electrocardiograms. A comparatively long graphic record was made, part of which, reproduced in Fig. 11, is characteristic of the entire curve and shows three groups in each of which there are three slow and three rapid beats. Seven groups of slow beats occurred in the entire tracing, and either three, four or five rapid beats occurred between them. The measurements of the lengths of all the cardiac cycles, as measured from the brachial tracing, are tabulated.

TABLE I.  
LENGTH OF CARDIAC CYCLES IN SECONDS.

Measured from the brachial tracing in Fig. 11 and in the remainder of the curve.

| CYCLES OF THE SLOW RHYTHM   |      |      | CYCLES OF THE RAPID RHYTHM.  |      |      |      |      |
|-----------------------------|------|------|------------------------------|------|------|------|------|
| 1st                         | 2nd  | 3rd  | 1st                          | 2nd  | 3rd  | 4th  | 5th  |
| 0.89                        | 0.94 | 0.80 | 0.59                         | 0.56 | 0.56 | —    | —    |
| 0.88                        | 0.92 | 0.82 | 0.60                         | 0.60 | 0.62 | —    | —    |
| 0.90                        | 0.93 | 0.85 | *                            | *    | *    | —    | —    |
| *                           | 0.89 | 0.83 | 0.61                         | 0.58 | 0.57 | 0.61 | 0.67 |
| 0.92                        | 0.96 | 0.85 | 0.61                         | 0.57 | 0.58 | 0.61 | —    |
| 0.91                        | 0.93 | 0.88 | 0.60                         | 0.56 | 0.59 | 0.63 | 0.65 |
| 0.91                        | 0.95 | 0.81 | 0.61                         | 0.57 | 0.55 | —    | —    |
| Average 0.90                | 0.93 | 0.83 | 0.60                         | 0.57 | 0.58 | 0.62 | 0.66 |
| Average Rate 67 per Minute. |      |      | Average Rate 102 per Minute. |      |      |      |      |

\* Cycles occurring in part of tracing that was missing.

From the table it is seen that the remarkable duplication of the groups is not confined only to their regular recurrence, but is noticeable also in the lengths of the various corresponding cycles, especially in the slow beats. The second beat of each group is longer than the others, while the third is the shortest, and the length of the corresponding beat in each group is strikingly constant. In the group of rapid beats, the second beat is usually a little shorter than



the first, and a tendency for the beats to lengthen, as the rapid group progresses, is seen, especially when the rapid group is composed of four or five cycles. These details indicate the definite rhythmicity in the changes in rate which occurred.

The jugular tracing in Fig. 11 shows three pairs of large unusual waves which accompany in each instance the last two of each group of slow beats. Between these pairs of waves, four cardiac cycles are seen, each represented by the usual *a*, *c* and *v* waves. These two series of normal waves have a very close resemblance to each other. The points in the venous tracing which are synchronous with the onset of the brachial pulse (marked *b*) always fall not only just after the onset of the normal *c* waves, as is to be expected, but also after the onset of the large unusual waves as well, at about the same length of time. As there is no evidence of auricular activity before these waves, it seems clear that the onset of these large waves represents the *c* wave, and that they are produced by ventricular activity. There are prominent waves following closely and partially fused with the *c* waves which undoubtedly represent auricular activity. The occurrence then of the waves in the venous tracing which are caused by auricular contractions, marked *a*, is not regular, and it is evident that after every four or five normal cardiac cycles, conspicuous slowing of the auricular rate takes place. The slow auricular rate continues for only two beats. During these two beats the ventricular systoles do not follow but precede the auricular systoles, the *c* waves preceding the *a* waves in the venous tracing.

The electrocardiogram (Fig. 12) shows a group of two slow auricular intervals (*P-P* time), followed by seven rapid beats. The relation of the *R* waves to the *P* waves during the auricular slowing is abnormal. The onset of the *R* wave is abnormally close to the onset of the *P* wave, sometimes practically coinciding with it. This relation makes it evident that the ventricular contractions during the slow beats are not dependent for their stimuli upon the auricular activity.

#### *Discussion of the curves.*

These curves show two abnormal factors which together determine the form of the rhythmic change in the cardiac activity. The first is a periodic change of rate of the auricular contractions. The second is the occurrence of an abnormal relation of the auricular and ventricular contractions during the periods of slow auricular activity. Each factor needs to be discussed separately.

(1) *The rhythmic change in the auricular rate* is associated in this case apparently with the administration of digitalis, as it occurred only after the patient was well under the effect of the drug, and disappeared several days after the drug was stopped. The tracing of the respiratory movements, taken synchronously with the electrocardiogram, shows that the sudden

slowing of the auricular rate bears no relation to respiration. This observation is in accord with that of Turnbull<sup>20</sup> who observed marked changes in rate of the whole heart, independent of the respiratory movements, following the use of squills, which he considered as dependent on changes in vagus tone. There was also in his case considerable depression of conductivity leading to partial heart-block.

The rhythmic changes of rate which occurred in our case seem very probably to have resulted from the action of the drug on the heart through the vagi. It is well known that digitalis acts on the heart, at least in part, through its ability to raise the vagus tone, but usually the increase of vagus action has a more marked inhibitory effect on the conductivity than on the rhythmicity of the heart. There is, in fact, considerable evidence for the belief, especially emphasized by Cushny,<sup>2</sup> that the therapeutic value of digitalis depends largely upon its ability to lower conductivity. In this case conductivity was not lowered, as the *P-R* interval in the electrocardiogram never exceeds 0.17 sec., which is within the normal limits. The drug has then apparently produced a disturbance in rhythmicity without affecting conductivity.

(2) *The abnormal relation of the auricular and ventricular contractions* during the periods of slow auricular rate is seen in both the venous tracings and in the electrocardiograms. As has been pointed out, during these periods the ventricular contractions are not dependent for their stimuli upon the auricular contractions. It is clear also that the auricular and ventricular systoles in the slow cardiac cycles are not the result of fixed ectopic stimulus formation common to both, as it is indicated in both the venous tracings and the electrocardiograms that the relation of these activities to each other is not constant. The fact also that the *P* wave of the electrocardiogram in these abnormal cycles is not deformed shows that the course of the contraction through the auricle is normal. The ventricular complexes are also not deformed. It is clear, therefore, that the impulses for their contractions arise in some point between the auricles and the ventricles and passes to the latter in a normal manner. The curves indicate, therefore, that the stimulus formation for the ventricles is taken up by some independent point which possesses an inherent rate of rhythmicity higher than that of the auricles during their slow periods, and ventricular contractions result.

The inherent rate of the point which becomes the pace-maker of the ventricles when they beat independent of the auricles, is in this instance about sixty beats per minute. The action of digitalis had no effect on the inherent rate of this point, as ventricular contractions at the same rate appeared when the patient was free from the effect of the drug and when the auricular rate was slowed by pressure on the right vagus nerve. The curves showing this result of vagus pressure in this case were published in a previous communication<sup>15</sup> (Fig. 12-15). Although nothing is known as to the rate at which the ventricles of a normal child of seven would beat independently



of the auricles, it seems very likely, from what is known in general of independent ventricular rhythmicity, that this rate of sixty beats per minute is abnormally high. An even higher inherent ventricular rate has been encountered in two other cases of endocarditis in children, in which the ventricles beat spontaneously whenever the auricular rate was sufficiently slowed by stimulation of the right vagus nerve. These cases have been discussed in a previous paper.<sup>15</sup> The curves showing this dissociation resemble in form those obtained by Rothberger and Winterberg<sup>17</sup> during right vagal and left accelerator stimulation in dogs. In their experiments the vagus stimulation lowered the rate of the heart-beat as set by the sino-auricular node, while the accelerator stimulation raised the inherent rate of the ventricles, thus causing it to exceed that of the slowed auricles. In our cases the right vagus alone was stimulated, and we think that the ventricles established their independent rhythm because their inherent rate was raised by a constant abnormal activity of the accelerator nerves, or through a heightened susceptibility of the heart muscle to the action of the accelerators.

#### *Summary.*

The curves from a child of seven, suffering from chronic endocarditis, showed rhythmic changes in the heart-beat which were determined by two abnormal factors. First, there was a sudden and profound change in the auricular rate, occurring in a definitely rhythmic manner. This was apparently an effect of digitalis. Second, the ventricles beat independently of the auricles during the periods of slow auricular rate. This occurred because the inherent rate of the site of ventricular stimulus formation exceeded that of the retarded auricles. The actual rate was high, and was occasioned, we believe, by a hypertonus of the cardiac accelerator nerves or of a heightened susceptibility of the heart to the action of these nerves.

### PART III. (CASE 3.)

*History.* A physician, aged fifty-six, who lives in a high altitude and who is an active man, noticed about the year 1900 that he had occasional cardiac irregularity. This irregularity consisted of an intermission, occurring after a sequence of six or seven beats. At first, withholding tobacco for a few days seemed to induce more regular heart action. A trip towards sea level had the same effect. For a long period mental diversion, alcoholic stimulation or excitement seemed to bring about at once a slower and regular rhythm. The irregularity had become steadily more pronounced and when he was seen was not so amenable as formerly. Except for the discomfort of the sensations of cardiac irregularity, no serious inconvenience has been suffered. The patient had dizzy spells and tinnitus aurium at times for

many years, and on several occasions fainting attacks have been narrowly averted. Stabbing heart pains have occasionally been annoying. Tobacco had not been used immoderately, and he had taken very little alcohol.

The patient had scarlet fever at the age of ten and pneumonia at sixteen. He was very athletic in college between the ages of seventeen and twenty-one, and then turned suddenly to the sedentary life of a laboratory worker. About ten years after graduation, he developed pulmonary tuberculosis, from which he entirely recovered after five or six years. He had typhoid fever in 1896 after which he had a "typhoid rib," for which he was operated on (curetted). Healing required eighteen months.

*Physical examination.* Physical examination on June the 16th, 1911, showed practically nothing abnormal. When the patient sat, percussion demonstrated that the right cardiac border coincided with the left sternal margin. The superior outline of relative dulness lay in the third left interspace, and ran down 2.2 cm. to the left of the left nipple to the sixth interspace, 12.5 cm. to the left of the mid-sternum. The apex beat was under the sixth rib and in the sixth space, and its outer border being 12.5 cm. to the left of the mid-sternum. The first heart sound at the apex was impure and "scrapy," and the interval between the first and second sounds was abnormally short. The other sounds were clear. The pulse rate whilst sitting was 116 per minute, not counting frequent intermissions. The blood pressure (Janeway instrument) was 110 mm. mercury for the strong beats which came through the cuff after the pauses; the weaker beats forming the main part of the rhythm came through at about 104 mm.. The urine has always been normal.

*Description of curves.* The electrocardiograms (Fig. 13 and 14) were obtained after the patient had been smoking, and show groups of rapid beats divided from each other in a rhythmic manner by single prolonged cardiac cycles. The two curves differ from each other because the first was obtained with the second lead, the right arm and left leg, while the second was obtained by the third lead, the left arm and left leg. They differ also in that there are six beats (Fig. 14) in a group in one tracing and seven beats (Fig. 13) in a group in the other. In Fig. 13 (second lead), after a long diastole, a cycle occurs which is represented by a well defined positive *P* wave, a very small *R* wave, a well marked *S* wave and a low, rather elongated *T* wave. The unusual *R* wave is constant throughout the curve and its form need not concern us here. The *T* wave is apparently unchanged except by being deformed through partial coincidence with the wave that follows it. The important and striking change occurs in the *P* wave, which is reversed or negative in all the cycles which follow until the next pause. This change in the shape of the *P* wave indicates that the stimulus of contraction arises in some abnormal point and passes through the cardiac structures in an abnormal



fashion. In other words, the negative *P* wave indicates that it represents an ectopic auricular systole which by its rhythmic occurrence controls the heart rate.

A study of this curve reveals the following facts: After a pause of the heart in diastole, a cardiac cycle of normal sequence occurs. The diastole following this normal beat is short and is interrupted by an abnormal auricular systole, which stimulates a ventricular systole after a normal conduction time. Stimuli continue to arise at the abnormal point at a fairly rapid rate for five more beats, each followed by a ventricular contraction. Then a period occurs in which stimuli cease to be generated in the abnormal point, and a pause again occurs which allows the normal cardiac pace-maker to re-establish itself. The normal mechanism is dominant for one beat only, when the ectopic impulses again resume control.

The same mechanism is shown in Fig. 14, except that the pause occurs after five rapid beats instead of after six. The lengths of the cardiac cycles, as measured from the beginning of one ventricular systole to the next, vary considerably, and fall into three groups. The long cardiac cycles which include the pauses average 1.03 seconds in length and indicate a heart rate of 58 beats a minute. The first cycles after the pauses average 0.55 seconds in length and indicate a rate of 109 beats a minute, while the remaining beats of the groups average 0.45 seconds in length, indicating a rate of 133 beats per minute. Besides the rhythmic occurrence of beats belonging to these three groups, the beats of each group have a tendency to shorten as the end of the group is approached. As all these beats arise from the same abnormal point of stimulus formation, it is evident that the rate of stimulus formation gradually increases until for some reason the abnormal stimuli suddenly cease. This sudden cessation suggests that fatigue sets in and that rest is necessary before the function of stimulus formation can be resumed. It is probable, therefore, that a rhythmic alteration in the excitability occurs in some auricular region which is capable of generating stimuli, and that the change in excitability is determined by periods of rest and fatigue of the heart muscle itself.

### *Summary.*

The curves from this healthy man of fifty-six show rhythmic changes in the heart-beat which are caused by the fact that an abnormal auricular region generates stimuli at a rate faster than that of normal stimulus formation. The region therefore becomes the cardiac pace-maker, a function which it seems unable to maintain constantly. After a series of five or six abnormally rapid beats, this ectopic pace-maker fails to produce stimuli and a pause in its activity occurs, during which one normal cardiac cycle is developed. During this pause rest allows the abnormal pace-maker to resume its stimulus-forming function which ceases again after the same number of beats as before, on account of fatigue of the heart muscle itself.

## GENERAL DISCUSSION.

In the three cases that have been described, the feature common to all is the rhythmically recurring changes in the heart-beat. Such striking phasic changes are apparently rare. There is one form of rhythmic change in the rate of the ventricular contractions, however, which is not very infrequent and which occurs in partial heart-block. It is produced when every third or fourth auricular systole fails to stimulate a ventricular systole and when the conduction time in a group of beats shows progressive lengthening until the block occurs. Partial heart-block due to digitalis frequently exhibits this condition.

Rhythmic changes in the heart-beat were first experimentally investigated by Luciani,<sup>12</sup> who studied the periodic action of the suspended frog's heart under numerous conditions. Some of the curves show fairly definite rhythmic changes. Among others, Öhrwall<sup>13</sup> and later Langendorff<sup>6</sup> have discussed these peculiarities of heart action which are associated especially with certain stages of partial cardiac asphyxiation. Öhrwall considered that changes in the heart muscle, especially in excitability, underlay the rhythmic changes, while Langendorff thought that changes in the controlling nervous mechanism were probably primarily responsible. The cardiac action of the cases here described is quite different from the so-called Luciani periods. We have recently obtained electrocardiograms of what seem to be true Luciani periods in the human heart from dying patients, and they show groups of beats of the whole heart, followed by pauses sometimes a full minute in length. These observations have been described in detail in another communication.<sup>14</sup>

Wenckebach<sup>22</sup> has drawn an analogy between the cardiac rhythm observed in a patient and the Luciani periods. His case resembles superficially our first case. The details of the venous curves are not entirely clear, owing to the rapidity of the cardiac rate, but it is almost certain that the periodic changes of rate affected the whole heart and auricular extrasystoles played no part. In this respect his case does resemble more closely the Luciani periods than do ours. Wenckebach interprets the periodic changes in rate as caused by depression of excitability and rhythmicity of the heart through the activity of the cardiac nervous mechanism. It is an example of rhythmic changes in the heart-beat which is different from any we have observed.

A case resembling closely our second case has been described by Lewis.<sup>11</sup> The patient was under the influence of digitalis and the rhythmic changes of rate seemed to result from its action through the vagi. Not only rhythmicity but also conductivity was disturbed, however. With the slow auricular rate the ventricles inaugurated their own contractions, just as occurred in our case. Belski<sup>1</sup> has also published a curve (Fig 9) resembling the polygraphic tracings from our second case. Except for rhythmic changes produced by regularly recurring extrasystoles, such as that reported by Laslett,<sup>7</sup> no other forms of rhythmic changes in the human heart-beat have been described, so far as we know.



*The relation of our cases to other forms of arrhythmia.*

The classification of the cardiac arrhythmias in general use, that advocated by Hering,<sup>4</sup> offers no satisfactory place for these now described, although extrasystoles, auricular in the first and third and ventricular in the second, play a rôle in all. They cannot be considered, however, as extrasystolic arrhythmias in the usual sense.

A more interesting consideration is the relation which the first and third cases have to paroxysmal tachycardia. Largely through Lewis' <sup>8, 9 & 10</sup> work it now seems clear that the paroxysms of tachycardia occur when some region of the heart outside of the sino-auricular node takes over the function of impulse formation. This ectopic impulse formation becomes apparent only when the impulses are generated at a rate higher than that of the sino-auricular node, for only then does the abnormal region become the cardiac pace-maker.

In the first and third cases presented in this paper, a rapid cardiac rhythm occurs when a site originating ectopic auricular systoles stimulates the ventricular contractions. An abnormal activity of the accelerator nerves may here play a part in determining the ectopic auricular activity which becomes the cardiac pace-maker for short, interrupted periods. There is in one of these cases some evidence that the accelerators were abnormally active. There is also experimental evidence that the rate of stimulus formation may be raised by accelerator stimulation in abnormal regions above that of the sino-auricular node. Thus Hering<sup>4</sup> has found that accelerator stimulation may not only quicken the heart-beat, but may produce tachycardia. Rothberger and Winterberg have shown that accelerator stimulation raises the rate of rhythmicity of points in the ventricles of hearts poisoned by barium and calcium above that of the sino-auricular node, thus producing ventricular tachycardia. Possibly the normal pace-making region works usually relatively near its maximum rate, while other regions may be raised by influences outside of the heart itself, especially by stimulation of the accelerator nerves, to a much higher rate of rhythmicity than is normally present. Although the mechanism underlying each of these two cases may be the same as that underlying paroxysmal tachycardia, the rate of the rapid beats is not so high as usual, nor is it constantly maintained.

## GENERAL SUMMARY.

In the three cases that are described, changes in the heart rate have been observed by graphic records which occur in a rhythmic manner. The phasic character of these changes is the only feature common to all. In the first case the rhythmic change was the result of the alternating success and failure of ectopic auricular systoles to stimulate ventricular contractions. In the second case the auricular rate changed rhythmically and became periodically so slow that the ventricles were able to inaugurate their own rhythm. The periodic changes in auricular rate resulted from the administration of digitalis. In the third case ectopic auricular systoles occurred in

groups at a rate more rapid than that of the normal sino-auricular rhythm, and the site from which they arose became periodically the cardiac pace-maker.

The two cases in which ectopic auricular systoles periodically became the cardiac pace-maker are apparently closely allied to or identical with paroxysmal tachycardia so far as the mechanism underlying the abnormal cardiac action was concerned.

In the first two cases the nervous mechanism controlling the heart-beat seemed to be abnormal and played an important but not an exclusive rôle in the production of the rhythmic changes. In the third case, although there is less evidence of such an abnormality the sudden appearance of the unusual cardiac activity suggests that here also the nervous controlling mechanism was a factor in determining its onset.

#### BIBLIOGRAPHY.

- <sup>1</sup> BELSKI. "Beobachtungen über atrio-ventriculäre Automatie im Verlauf der Infektionskrankheiten." *Zeitschr. f. klin. Med.*, 1909, **LXVII**, 515.
- <sup>2</sup> CUSHNY. "Irregularity of the Heart and auricular Fibrillation." *Amer. Journ. med. Sci.*, 1911, **CXLI**, 826.
- <sup>3</sup> HERING. "Zur Analyse der paroxysmal Tachykardie." *München. med. Wochenschr.*, 1911, **LVIII**, 1945.
- <sup>4</sup> HERING. "Die Diagnose der Herzunregelmässigkeiten ohne Kurvenaufnahmer." *München. med. Wochenschr.*, 1908, **LV**, 2429.
- <sup>5</sup> HUNT. "Direct and reflex Acceleration of the mammalian Heart with some Observations on the Relations of the inhibitory and accelerator Nerves." *Amer. Journ. of Physiol.*, 1899, **II**, 395.
- <sup>6</sup> LANGENDORFF. "Untersuchungen über die Natur des periodisch-aussetzenden Rhythmus, insbesondere des Herzens." *Archiv. f. d. ges. Physiol.*, 1908, **CXXI**, 54.
- <sup>7</sup> LASLETT. "The regular Occurrence of interpolated Extrasystoles." *Heart*, 1909-10, **I**, 83.
- <sup>8</sup> LEWIS. "Paroxysmal Tachycardia." *Heart*, 1909-10, **I**, 43.
- <sup>9</sup> LEWIS. "The experimental Production of paroxysmal Tachycardia and the Effects of Ligation of the coronary Arteries." *Heart*, 1909-10, **I**, 98.
- <sup>10</sup> LEWIS. "Paroxysmal Tachycardia, the Result of ectopic impulse Formation." *Heart*, 1909-10, **I**, 262.
- <sup>11</sup> LEWIS. "Irregular Action of the Heart in mitral Stenosis: the Inception of ventricular Rhythm, &c." *Quart. Journ. Med.*, 1908-09, **II**, 356.
- <sup>12</sup> LUCIANI. "Eine periodische Function des isolirten Froschherzens." *Arbeiten aus d. physiol. Anstalt zu Leipzig*, 1873, **VII**, 113.
- <sup>13</sup> ÖHRWALL. "Ueber die periodische Function des Herzens." *Skand. Archiv. f. Physiol.*, 1898, **VIII**, 1.
- <sup>14</sup> ROBINSON. "A Study with the Electrocardiograph of the mode of Death of the human Heart." *Journ. exper. Med.*, 1912, **XVI**, 291.
- <sup>15</sup> ROBINSON AND DRAPER. "Studies with the Electrocardiograph on the Action of the vagus Nerve on the human Heart." *Journ. exper. Med.*, 1912, **XV**, 14.
- <sup>16</sup> ROSENTHAL. "Report of a Case demonstrating Pulsus Alternans, blocked auricular Extrasystoles and aberrant ventricular electric Complexes." *Amer. Journ. med. Sci.*, 1911, **CXLII**, 788.
- <sup>17</sup> ROTHBERGER AND WINTERBERG. "Ueber die Beziehungen der Herznerven zur Atrioventriculären Autonomie (Nodal Rhythm)." *Archiv. f. d. ges. Physiol.*, 1910, **CXXXV**, 559.
- <sup>18</sup> ROTHBERGER AND WINTERBERG. "Ueber die Beziehungen der Herznerven zur automatischen Reizerzeugung und zum plötzlichen Herztode." *Archiv. f. d. ges. Physiol.*, 1911, **CXLI**, 343.
- <sup>19</sup> ROTHBERGER AND WINTERBERG. "Ueber die experimentelle Erzeugung extrasystolischen ventrikulären Tachycardie durch Acceleransreizung." *Archiv. f. d. ges. Physiol.*, 1911, **CXLII**, 461.
- <sup>20</sup> TURNBULL. "Cardiac Irregularities produced by Squills." *Heart*, 1910-11, **II**, 15.
- <sup>21</sup> WENCKEBACH. "Ueber eine kritische Frequenz des Herzens bei paroxysmaler Tachykardie." *Deutsch. Archiv. f. klin. Med.*, 1910, **CI**, 402.
- <sup>22</sup> WENCKEBACH. "Beiträge zur Kenntnis der menschlichen Herztätigkeit." *Archiv. f. Anat. u. Physiol.*, 1908, *Physiol. Abth.*, Suppl., 53.



4.

5.

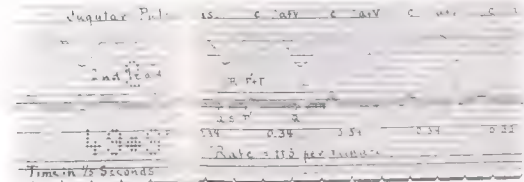
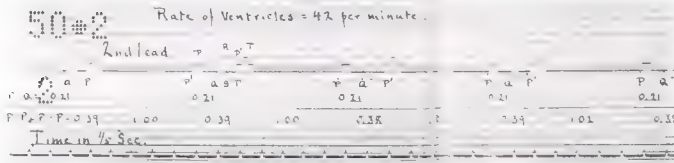
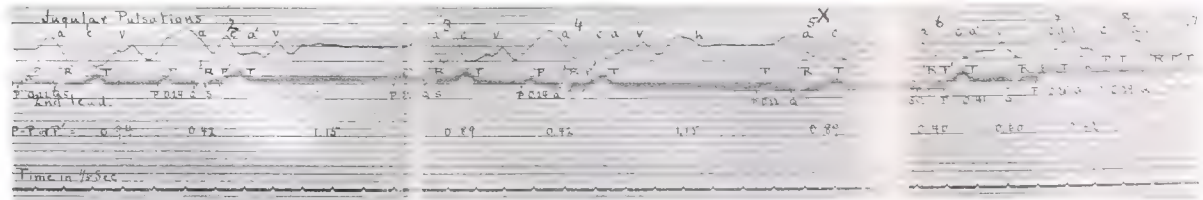
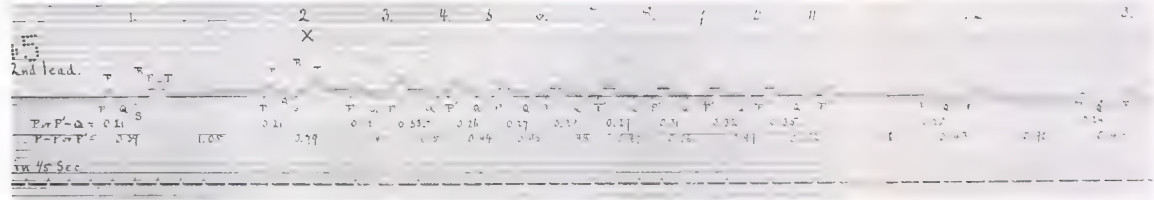
be

6.

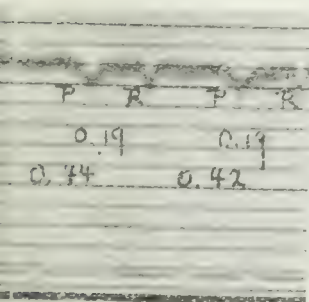
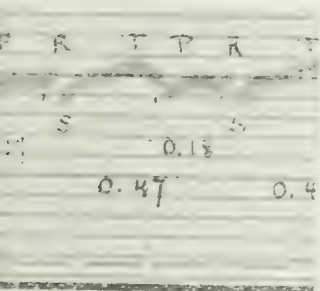
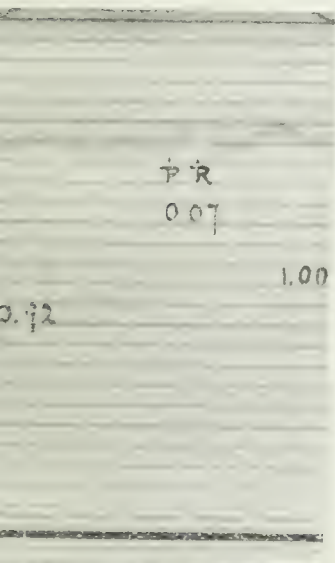
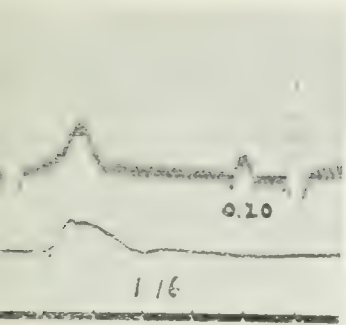
sy

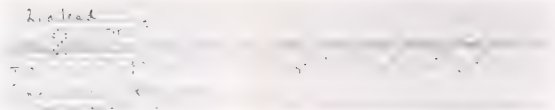
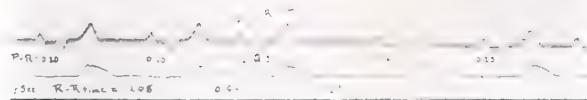
8.

re



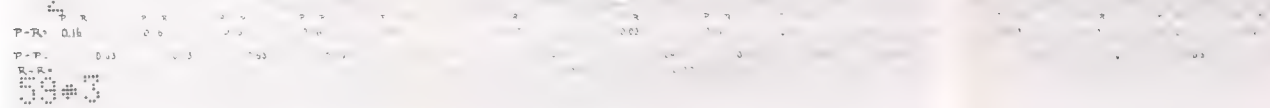






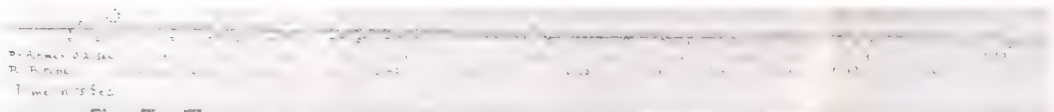
Respirations Down stairs - 1st floor

2nd lead



Time in 1/5 Sec

2nd lead  
P-R = 0.14  
Q-T = 0.10  
R-R = 0.03  
Time in 1/5 Sec





## EXTRASYSTOLE AND THE STAIRCASE PHENOMENON.

By E. W. GOTELING VINNIS.

(*The Hague*).

I WISH to draw attention to a very curious occurrence, which I had occasion to observe in examining a patient under my care for attacks of paroxysmal tachycardia. He is a man of nearly sixty years of age, and has suffered from these attacks for about forty years, being otherwise quite healthy. The attacks were of the ordinary auricular form, as may be easily seen in the tracing (Fig. 1), where the auricular wave *a* is clearly visible.

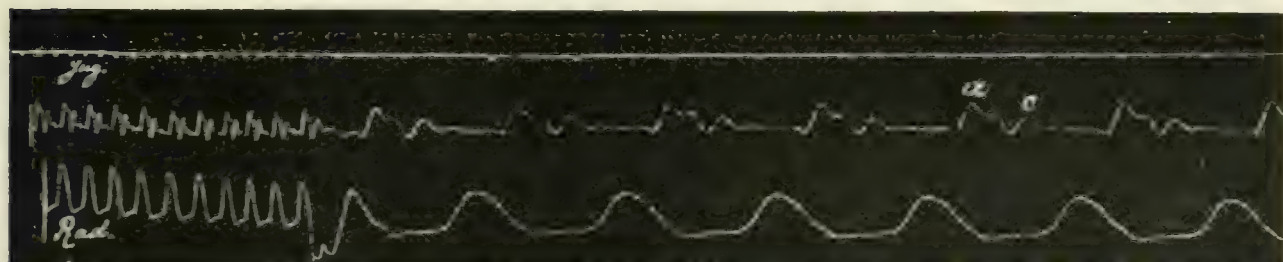


Fig. 1. Jugular and radial curves during attack of paroxysmal tachycardia. Pulse rate, 180.

The attacks came about once a month, with some regularity; left to themselves they would sometimes persist for thirty hours and more, after an intramuscular injection of Digalen (3 cc.) they invariably stopped after an hour or two.

So far as I have related it the case does not present any unusual feature. During an interval between attacks the patient, who usually felt quite well at such times, came to me because he felt some disagreeable sensation of *irregular* heart-action. (I must mention here that during the intervals he took no cardiac tonic, but for the last week had taken small doses of iodide of potassium.)

Now extrasystoles were not uncommon in this patient. I had observed them in him many times before; they were, as a rule, of the ventricular type after attacks of tachycardia, though otherwise usually of the auricular type as could be expected in a sufferer from paroxysmal tachycardia. But it seemed that this irregularity which he would hardly notice at other times now disturbed him to a certain extent. Therefore, after feeling the pulse and noticing several "dropped beats," I took a tracing, which to my surprise, presented the features reproduced in Fig. 2.

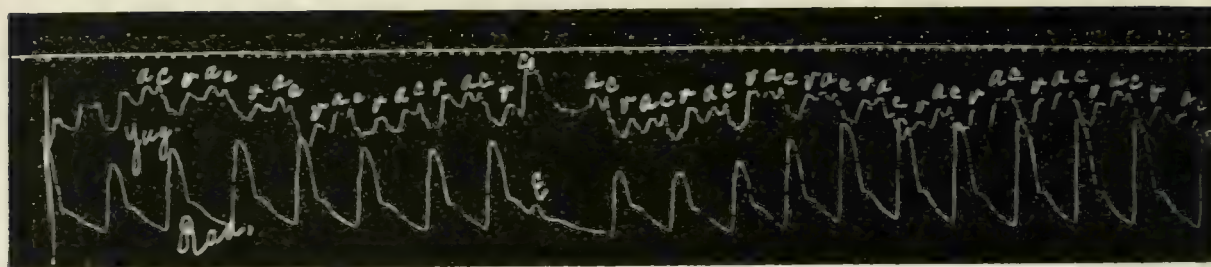


Fig. 2. Jugular and radial tracing, presenting extrasystole, followed by staircase.

It will be seen that there is a ventricular extrasystole *E*, which gives a very slight elevation in the radial pulse, while in the jugular tracing the corresponding wave  $c_1$  coincides with the *a* wave, which comes exactly at the time. The following radial pulse comes exactly at the anticipated point; there is a full compensatory pause; there is no disturbing of the function of conductivity as the *a-c* interval is the same throughout and never exceeds one-fifth of a second. But where we are led to expect the following wave in the radial pulse to be larger than usual, here we see very clearly that it is much smaller. After this there is a regular and gradual increase, till after five or six beats the waves are as large as might have been expected of the first beat after the pause, then a gradual decrease to the normal strength is visible. Happily I was able to verify this phenomenon (which, by the way, was absolutely independent of breathing) in more than one instance. As the phenomenon is in a measure paradoxical and, so far as I know, in this connection has never been described before, I give tracings of two other periods in which the same features are easily recognised (Fig. 3 and 4).

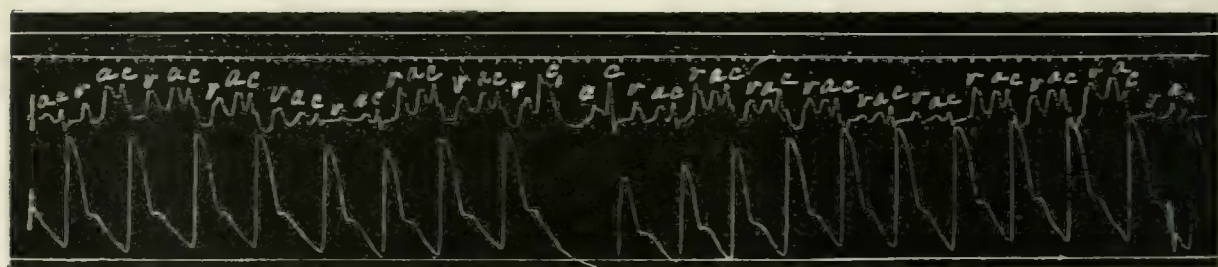


Fig. 3. Venous and radial pulse, showing extrasystole, followed by staircase.

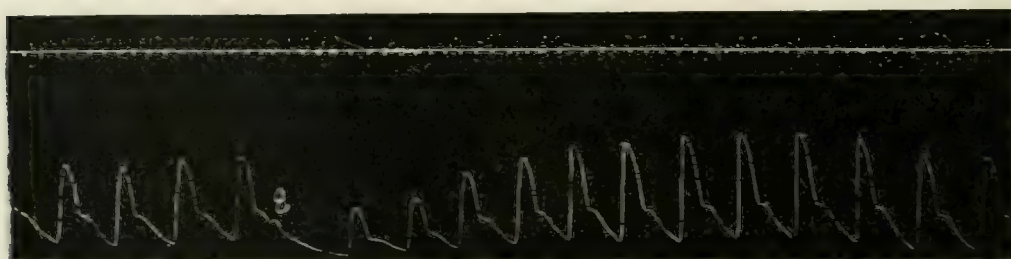


Fig. 4. Radial tracing, showing extrasystole and very striking staircase.



In Fig. 4 the venous pulse is not given. It is reproduced because the phenomenon is still more striking here than in Fig. 2 and 3.

The curves 2-4 present a perfect resemblance with those known in physiology as showing the "staircase phenomenon" and first observed by Bowditch, whose name has since been connected with it. In experiment it is sometimes (not as a rule) seen after vagus-stimulation, when this has first effected a standstill of the heart. Gaskell thinks it can be produced in two ways: first because the contractility has been so affected that it needs some time to perfectly restore itself; second, because the action of the heart-cavity under observation begins with a partial contraction and only gradually extends over all the muscle fibres. Mackenzie in his "Diseases of the Heart" gives some instances of the staircase occurring clinically after a standstill of the whole heart under the influence of digitalis; clinical observations presenting the phenomenon after an ordinary extrasystole have, so far as I know, never been published. It seems difficult to say which of the two possibilities put by Gaskell may be the cause of the staircase as I observed it here. First we should notice that, so far as can be judged from the jugular tracings, the phenomenon is confined to the ventricle, the *a* wave presenting no striking differences in size.

I should be inclined to think that here we have an affection purely of contractility; chiefly because the pulse waves gradually increase so far as to become larger than usual, while in a man, who as a rule lived as a perfectly healthy person, we cannot suppose that the beats of usual size should be effected by an imperfect ventricular contraction. It would also be difficult to suppose that a contraction extending gradually over the different muscle fibres would produce such a *regular* staircase, because in the ventricle of the human heart the muscle fibres are largely differentiated as to their functions and contribute by no means in an equal measure to the propelling of the blood.

If the staircase then must be ascribed to an impairment of the function of contractility, we come to the question how it was that this function, which as a rule in this patient showed no signs of being in any way affected, came suddenly to be disturbed. Here I should like to draw attention to a paper of Rihl,<sup>1</sup> who first doubted if the ordinary *increase* of the "postextrasystolic systole" was only produced by the longer pause and the more ample restoration of functions during the longer rest, combined with the greater filling of the ventricle with blood. Rihl came to the conclusion that there must be another factor; chiefly on account of observations where the pause after an extrasystole was not longer or even shorter than usual and where the increase in size of the following beat was nevertheless obvious. He assumes that a premature beat as such has a power of increasing the function of contractility for the following beat. Sometimes even the two or three following beats may thus become stronger than usual. It is, however, more common to see the contractility affected so that the second beat after the extrasystole is smaller than its predecessor, or even smaller than the ordinary beats, from



which a sort of "pulsus alternans" may result for some beats; a phenomenon which has been taken by Mackenzie and others as *signum mali ominis*.

Before Rihl, Woodworth,<sup>2</sup> although giving no definite explanation, had already seen an analogy between the increase of the postextrasystolic beat and the staircase phenomenon, and even went so far as to call it "a fresh example of the staircase phenomenon," a somewhat daring supposition because in his cases the "staircase" had only one step. My observations, however, seem to show that he was not altogether in the wrong. As an exception we here have the reversed influence of the premature beat on the function of contractility; notwithstanding the longer pause there is a decrease of this function, which only gradually gives place to the usual effect of increase. An analogy with normal and abnormal *reflex* phenomena (the most popular is perhaps that of Babinski) is obvious. Here the premature beat seems to act as a stimulus, which by a nervous reflex affects the contractility, in this case by depressing it, as a rule by increasing it, which by analogy may now safely be assumed.

A reflex needs some easily measurable time to produce its full effect and I am glad to be able to give a tracing taken from the same patient on the same day, where this seems to be more clearly shown. In Fig. 5 the extrasystole

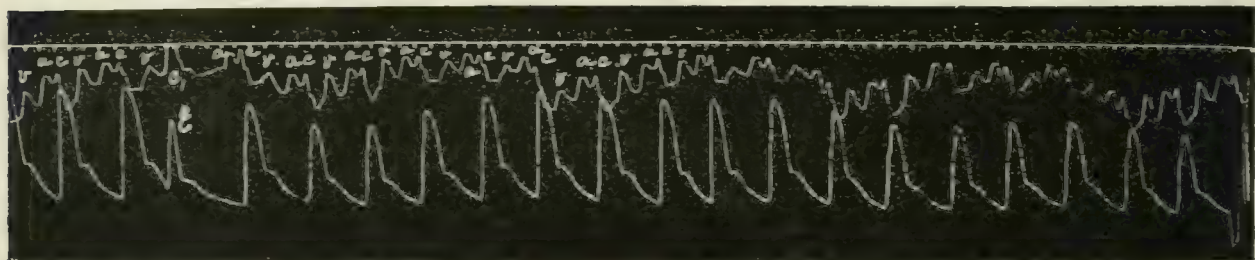


Fig. 5. Jugular and radial tracings showing staircase, first falling, then rising after a premature beat.

occurs somewhat later in the period, as shown by the greater elevation in the radial tracing. Now here the following beat is only a little smaller than the ordinary beats and we see that the full effect of the reflex, which affects the contractility, is shown only in the second and third beats, after which the gradual increase is seen as in the other tracings. In "reversed" analogy with this observation are the observations of Rihl, that the increase of the postextrasystolic beat is stronger in proportion as the extrasystole is more premature. The curve of Fig. 5 seems also to preclude any explanation which might attribute the decrease of the beats to a simple exhaustion of the heart-muscle after the atypical and perhaps forcible contraction of the extrasystole; in this case the beat immediately following the extrasystole should always be the weakest.

As the staircase phenomenon is produced in experiment by vagus stimulation, we are inclined to think that here also the extrasystole acted as a stimulus for a *vagus* reflex. If this be true, it is very curious to see how



strictly the vagus-action is here confined to the function of contractility of the ventricle, while the conductivity and stimulus production are not affected at all; and these observations may be taken as another instance for the independence of the different functions of the heart, even for the independence in action of the different vagus-fibres. In fact we are more and more compelled to consider the vagus not as a single nerve but as a quantity of nerves with very different functions, included in one "reservoir."

I give these observations without further speculation, as I think they might be of some interest. I will not omit to say, however, that the day after the taking of these tracings the patient had a short attack of paroxysmal tachycardia and that afterwards the phenomenon was no more observed.

#### REFERENCES.

- <sup>1</sup> RIHL. "Zur Erklärung der Vergrößerung der postextrasystolischen Systole des Säugetierherzens." *Zeitschr. f. exper. Pathol. u. Therap.*, 1906, III, 1.
- <sup>2</sup> WOODWORTH. "Maximal Contraction, staircase Contraction, refractory Period and compensatory Pause of the Heart." *Amer. Journ. of Physiol.*, 1903, VIII, 213.

## PAROXYSMAL TACHYCARDIA.

THE PAROXYSMS ARISE FROM IMPULSES OF VENTRICULAR ORIGIN. THE AURICLE RESPONDS TO THE VENTRICLE. EVIDENCE OF TWO POINTS OF ABNORMAL VENTRICULAR IRRITABILITY.

BY T. STUART HART.

(*New York*).

(*From the Second Medical Division of the Presbyterian Hospital*).

PAROXYSMAL tachycardias of ventricular origin are in our experience of rare occurrence, and a review of the literature<sup>5 & 6</sup> would seem to confirm us in this view. Of the seventeen cases of paroxysmal tachycardia of which we have been able to make more or less complete studies by graphic methods this is the only one in which the proof seems to be adequate that we are dealing with a condition in which the damaged ventricular musculature is the underlying cause of the paroxysms.

### *Clinical history.*

J. W., a married man of 49 years and a native of Ireland was a stone paver by occupation; he was admitted to the Presbyterian Hospital on February the 6th, 1912, complaining of "palpitation of the heart and insomnia."

Such family history as could be obtained had no bearing on his condition.

He had measles as a child. From time to time he suffered from aches and pains in the arms, legs and back, but there is no clear rheumatic history. He thinks he had a "chancre" thirty years ago; he was treated for this for two weeks only, but seems to have had no secondary symptoms. He had two attacks of gonorrhœa twenty-eight years ago. His work has always been the heaviest kind of labour. Until two years ago he consumed large amounts of alcoholic beverages (ten to twelve drinks a day; beer and whiskey).

For a year he has been troubled with palpitation and dyspnœa on climbing stairs, but has had no pain. About six weeks ago he began to be awakened at night by the loud beating of his heart, after awakening he had great difficulty in getting to sleep on account of the palpitation although he was very sleepy; he would get up and smoke and this would make him cough and he became more comfortable than before. During the last week the attacks have been coming on each night and he has slept very little.



For two weeks he has had a cough with mucous expectoration. He has never suffered from œdema of the legs. For the past two months he has had a number of "dizzy spells" especially when at work, these have been more frequent during the past two weeks. He feels pretty well during the day time and able to work. His bowels are regular: the appetite is poor.

*Examination on admission* showed a thick-set man, well nourished and with no apparent dyspnœa or cyanosis; the mucous membranes were of good colour. The chest wall was thick, the lungs expanded poorly, the expiration was prolonged and a few fine râles were heard at the bases. The respiratory rate was 24.

The heart's apex beat was not palpable: there was dulness on percussion in the fifth space 12.5 cm. to the left of the mid-line: no dulness could be detected to the right of the sternal margin. The heart sounds were indistinctly heard, at the base the second pulmonic was louder than the aortic sound. During the periods of slow rate a soft blowing systolic murmur could be heard at the apex. The rhythm showed great irregularity, there would be a few regular beats at a rate of 80 to 90 a minute, frequently interrupted by premature beats followed by pauses, and again interrupted by a short period of rhythmic tachycardia at a rate of approximately 200 per minute. During the slow rate most of the heart beats could be felt at the wrist but during the rapid periods the pulse was at times nearly imperceptible and could not be counted.

The liver dulness extended from the fifth space to the costal margin in the right mid-clavicular line: the edge could not be felt. There was no œdema.

The urine averaged about 1,200 cc. per diem in quantity and showed no abnormality.

The blood was normal.

During the first 48 hours of his stay in the hospital the tachycardia was present most of the time, the paroxysms lasting from a few seconds to three minutes, with intervals of slower rate lasting from a few seconds to five minutes. This gave him much precordial distress and he slept very poorly. Under rest, bromides and a little digitalis the paroxysms of tachycardia gradually diminished in frequency and the heart action fell to 70 per minute, interrupted by frequent premature beats which for periods would give the pulse a bigeminal or trigeminal character. Even after the tachycardia had disappeared during the day time, he had occasional paroxysms at night and these persisted up to the time of his discharge on February the 20th.

Since leaving the hospital he has been seen a number of times. In spite of advice to the contrary, he has been employed in the heaviest kind of labour, hod carrying, &c., and feels perfectly well. At the times he has been seen no tachycardia has been detected and he is not conscious of palpitation. His pulse is usually about 70 and perfectly regular. When last seen on May the 19th an occasional premature beat was noted.

*The electrocardiograms of the slow periods.*

The records of the electrocardiograms and the radial pulse (Fig. 1, 2, 3), were taken during a period of slow heart action on a day (February the 13th) during which only two paroxysms were observed. This was what might be called his normal rhythm. The action is perfectly regular; the rate is 57 per minute.

The electrocardiogram in all three leads is extremely abnormal. *P* is present throughout, but is distorted in form, being composed of a double peak instead of the normal single elevation. The auricular complex is invariably followed by a ventricular complex but the *P-R* interval is considerably longer than the normal, measuring constantly 0.25 second. At this time the patient was getting a small amount of digitalis which undoubtedly increased the conduction time but records taken when he was not on digitalis or other medication constantly showed a *P-R* interval exceeding 0.2 second. This digitalis effect on susceptible hearts was first pointed out by Mackenzie<sup>11</sup> and has since been verified by many observers.

The ventricular complex is also abnormal. The departure from the normal complex consists mainly in a deformity of the *QRS* group; this is broad, measuring 0.17 second (for normal see 7), the summit is low and is made up of several more or less well marked oscillations. *T* is well defined in all leads. The ventricular complex occupies about 0.45 second. Diastole lasts 0.33 second.

It is evident that the musculature is so damaged that the passage of impulses is interfered with in all parts of the conducting system, some muscle fibres which should normally have terminated their activity before other muscle fibres become active are still under stimulation. The abnormal complex is probably to be explained not altogether on the assumption that the impulse takes an abnormal course through the conducting system, but on the ground that the abnormally long time consumed in the passage of the stimulus results in an unusual algebraic sum of the differences of electrical potential at a given moment.

This heart working at its greatest efficiency at a rate of 57 consumes so large a portion of the cardiac cycle for its systole that there remains only 0.33 second for its diastole, no longer a diastolic period than one would normally find in a heart beating at the rate of 72 per minute.

*Study of the paroxysms.*

The constitution of the paroxysms is shown very clearly in Fig. 4 and 5. To the right is seen the regular slow rhythm interrupted by a premature beat of ventricular origin (right basal type<sup>2 3 & 4</sup>) with complete compensatory pause. A comparison of the individual beats of the paroxysm with the single premature beats leaves no doubt that we are here dealing with a tachycardia which is composed of a series of ventricular premature beats arising from the same point in the wall of the heart as that from which the



single premature beats arose. The first beat of the paroxysm is clearly a premature beat entirely similar to those of isolated occurrence and this is followed by a series of like beats at nearly rhythmic intervals at a rate of 240 per minute. The onset of the paroxysm was always of the same type (Fig. 4 and 8). The offset showed considerable variation (Fig. 4, 5 and 8).

A close scrutiny of the isolated premature beats reveals quite constantly a notch in the descending limb at a point where the deflection becomes less rapid (Fig. 4) which we believe to be the representative of a reversed auricular activity due to the passage of the stimulus from the ventricle to the auricle. In many of the records of tachycardia this wave is quite evident (Fig. 4 and 8) but occurs with every second or third beat only. It is probable that during the tachycardia every other impulse from the ventricle to the auricle was blocked. This interpretation finds support in the work of Lewis<sup>10</sup> who has demonstrated that in ventricular tachycardias produced experimentally in the dog, alternate impulses of a reversed rhythm were blocked when the rate reached 220 per minute.

A comparison of the electrocardiogram and the radial pulse (Fig. 4 and 8) indicates clearly the lack of power of the premature beats, singly or in series, to maintain an adequate circulation.

Between the paroxysms the ventricular beats were often arranged for considerable periods in groups of three, each group consisting of two ordinary rhythmic beats and a premature contraction; or there might be coupling, the coupling consisting of an ordinary beat and a premature contraction, as shown in Fig. 5.

Another feature of the paroxysms which is well shown in a number of our records is *alternation*. Fig. 7 was taken during the latter part of a paroxysm which had lasted for about 2 minutes and on a day when he was having many attacks. The alternate complexes show considerable differences both in amplitude and duration. The explanation of alternation is still debateable, but authorities for the most part agree that it is significant of a gravely damaged ventricular musculature and that it is made evident by unusual demands upon such muscle.<sup>9 & 13</sup>

#### *Intermission.*

Fig. 6 presents a phenomenon which was occasionally recorded, viz., the dropping out of a complete beat: there is no evidence of either auricular or ventricular activity during the pause. This record was taken when the patient was not under the influence of digitalis, and when the rate of the heart action was 83. On the same day paroxysms of tachycardia were occurring at intervals of a few minutes. The pause is suggestive of a vagus effect.<sup>8 & 12</sup> In view of the exceptional irritability of the ventricle in this case and on this particular day, it is rather surprising that there is no escape of the ventricle during the long pauses.

On account of the length of this period which lacks only about 0.1 second of the length of two cycles of the ordinary rhythm, one is tempted

to suggest that we may here be dealing with a condition of sino-auricular block, but as we have no direct evidence of sinus activity this explanation can be entertained only on theoretical grounds.

*Two types of premature contractions of the ventricle.*

As improvement became more evident the heart beat presented periods of a rhythm of still another form. This is shown in Fig. 8 and 9. These records were taken after the patient had been in the hospital some days and when the paroxysms of tachycardia had become quite infrequent. As will be seen, a premature ventricular contraction of a new form appears (left sided apical<sup>2, 3 & 4</sup>). The presence of this type indicates another point of ventricular irritability near the apex. For considerable periods the two types of premature contractions occurred in a rhythmic series as follows :—

1. Usual beat.
2. Premature beat (apical type).
3. Usual beat.
4. Usual beat.
5. Premature beat (basal type).

This series was then repeated for a number of cycles. The premature beats of the apical type were only met with when mixed with the other beats in the stated order.

The diastolic pauses following each of the couples of the different types were of the same lengths. The premature beats of the basal type occurred nearly 0.1 second earlier in relation to the preceding beat than did the premature beats of the apical type, the former were superimposed on the preceding *T* wave, while the latter followed the termination of the preceding *T* wave. This fact suggests that the stimulation of the basal fibres at the time of the occurrence of *T* may have a causal relationship to the premature beat of the basal type.

*General remarks.*

The case of paroxysmal tachycardia presented offers evidence of a considerable degree of damage to various portions of the myocardium :—

1. Damaged auricular tissue (abnormal *P* complex, dropped beat).
2. Damaged junctional tissue (lengthening of *P-R* interval).
3. Damaged ventricular tissue (abnormal *QRS* complex, ventricular premature beats of two types, periods of tachycardia, composed of ventricular premature beats, alternation).



The ventricular tachycardia shows a remarkable parallel to the conditions produced in a dog by Lewis<sup>10</sup> when he tied the descending branch of the left coronary artery; the series of premature beats of ventricular origin, the auricular response to the ventricular pace-maker and a blocking of a part of these reversed stimuli, all have their counterparts in the case here presented.

It seems quite probable that in this case we are dealing with myocardial changes due to coronary disease possibly following a syphilitic infection and the prolonged use of alcohol.

## BIBLIOGRAPHY.

- <sup>1</sup> EINTHOVEN. *Archiv. f. d. ges. Physiol.*, 1908, cxxii, 517.
- <sup>2</sup> EPPINGER AND ROTHBERGER. *Zeitschr. f. klin. Med.*, 1910, lxx, 1-20
- <sup>3</sup> KRAUS AND NICOLAI. *Berl. klin. Wochenschr.*, 1907, xliv, 765 and 811.
- <sup>4</sup> KRAUS AND NICOLAI. *Deutsch. med. Wochenschr.*, 1908, xxxiv, 1-5.
- <sup>5</sup> KURE. *Deutsch. Archiv. f. klin. Med.*, 1912, cvi, 33.
- <sup>6</sup> LEWIS. *Mechanism of the Heart Beat*, London, 1911, 168.
- <sup>7</sup> LEWIS. *Mechanism of the Heart Beat*, London, 1911, 24.
- <sup>8</sup> LEWIS. *Mechanism of the Heart Beat*, London, 1911, 258..
- <sup>9</sup> LEWIS. *Mechanism of the Heart Beat*, London, 1911, 276.
- <sup>10</sup> LEWIS. *Heart*, 1909-1910, i, 100.
- <sup>11</sup> MACKENZIE. *Brit. med. Journ.*, 1905, i, 587.
- <sup>12</sup> MACKENZIE. *Diseases of the Heart*, London, 1908, Pl. iv, Fig. 259.
- <sup>13</sup> MACKENZIE. *Diseases of the Heart*, London, 1908, 188.

- Fig. 1. Electrocardiogram Lead I. Time 0.2 sec.. Regular, slow, rate 57. Abnormal *P*. Lengthened *P-R* interval. Abnormal *QRS* complex.
- Fig. 2. Electrocardiogram Lead II. Time 0.2 sec.. Regular, slow, rate 57. Delayed Conduction. Abnormal *P*. Abnormal *QRS* complex.
- Fig. 3. Electrocardiogram Lead III. Time 0.2 sec.. Regular, slow, rate 57. Abnormal *P*. Lengthened *P-R* interval. Abnormal *QRS* complex.
- Fig. 4. Electrocardiogram Lead III. Time 0.2 sec.. Single Premature beat. Tachycardia rate 240. Reversed *P*. Transitions.
- Fig. 5. Electrocardiogram Lead III. Time 0.2 sec.. Tachycardia. Bigeminus. Transition.
- Fig. 6. Electrocardiogram Lead III. Time 0.2 sec.. Usual complexes of slow rate. Dropped beat. Interval nearly equals time of two ordinary cycles.
- Fig. 7. Electrocardiogram Lead III. Time 0.2 sec.. Tachycardia. Alternation. Reversed *P*. Taken toward the termination of one of the longer paroxysms.
- Fig. 8. Electrocardiogram Lead III. Radial. Time 0.2 sec.. Two types of ventricular premature beats. Tachycardia. Transitions.
- Fig. 9. Electrocardiogram Lead III. Time 0.2 sec.. Rhythmic occurrence of two types of premature beats and ordinary complexes.



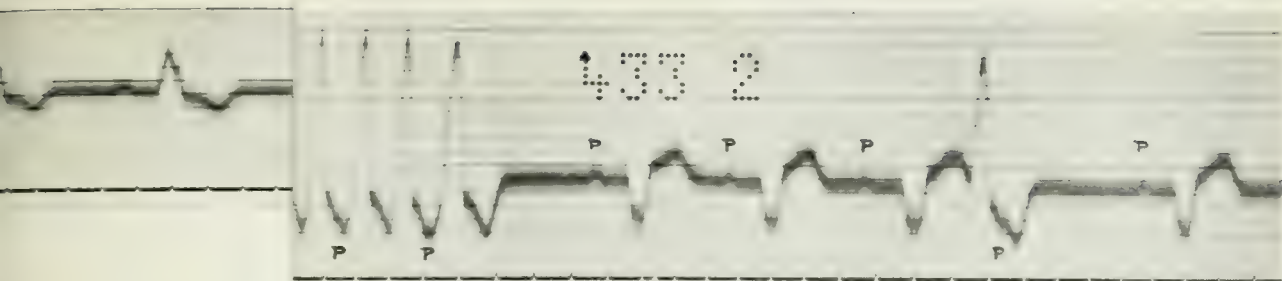


FIG. 4.

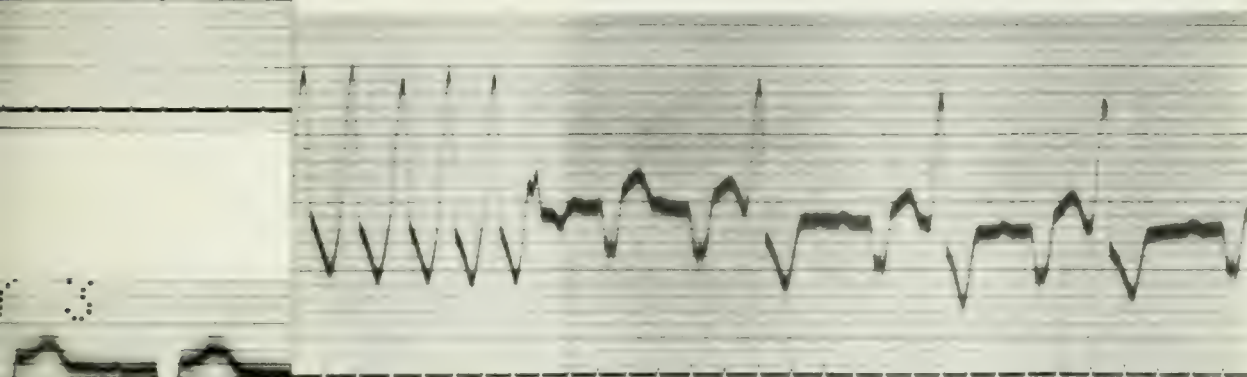


FIG. 5.

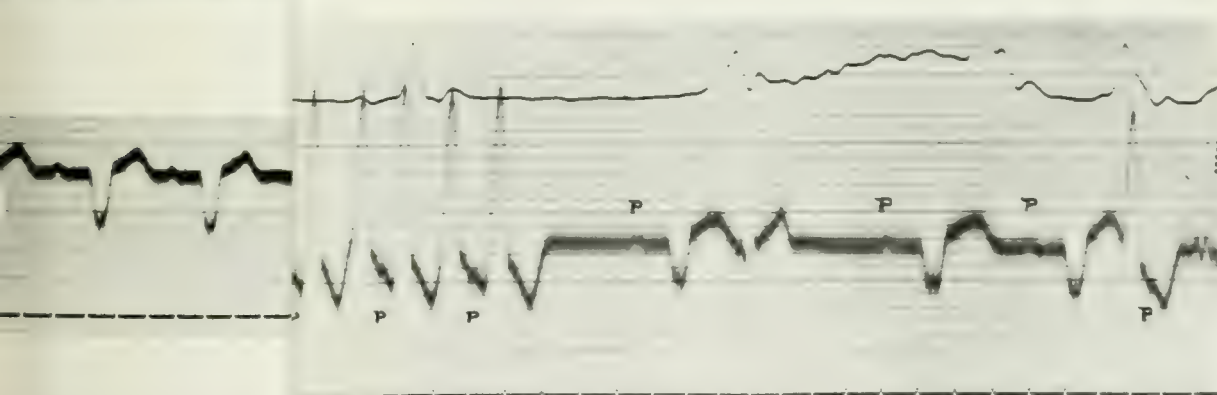


FIG. 8.

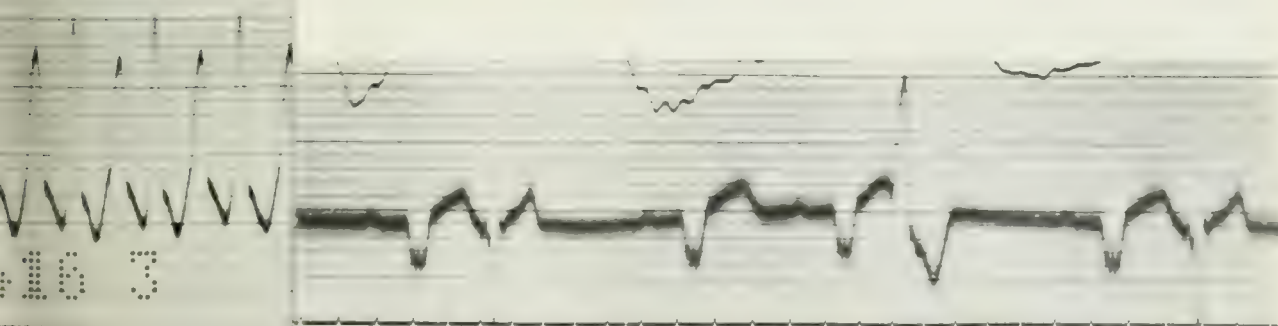
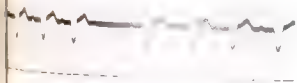
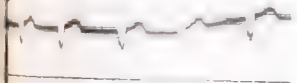


Fig. 9.





# OBSERVATIONS ON A CASE PRESENTING A LONG *a-c* INTERVAL, ASSOCIATED WITH SHORT PAROXYSMS OF TACHYCARDIA ARISING IN THE JUNCTIONAL TISSUES.

BY A. W. FALCONER AND GEORGE DEAN.

(Aberdeen).

THE following case was admitted into the Aberdeen Royal Infirmary on February the 29th, 1912, under Dr. Edmond, to whom we are indebted for the opportunity to observe the case.

*Past history and habits.* The patient was a baker aged 41. Twenty years before admission to hospital he had an attack of gonorrhœa, but there was no history of syphilis. He enlisted during the Boer War, and served three years in South Africa, where he contracted a severe attack of typhoid fever on account of which he was invalided home. He recovered from this and remained well until a year before admission, when he suffered from an attack of pneumonia from which he considered he never fully recovered. He had been a fairly heavy drinker. He never suffered from acute rheumatism.

*Present affection.* The patient never fully regained his strength after his attack of pneumonia. Six months before admission to hospital he began to be troubled with breathlessness, and his feet became swollen. His condition continued to get worse until his admission to hospital.

On admission he was found to be a poorly nourished man. There was conspicuous orthopnœa and generalised œdema. He was much troubled with cough, and expectorated a considerable amount of blood-stained sputum. The apex beat of the heart was situated in the fifth interspace about 1 inch outside the nipple line. At the aorta there was a loud systolic and a diastolic murmur. At the apex there was a systolic murmur, an early diastolic and a distinct crescendo presystolic murmur. At the tricuspid area there was a loud systolic murmur, which had a different quality from the systolic murmur heard at the apex. The pulse was of the water-hammer type and the rhythm varied from time to time. The lungs showed numerous crepitations at both bases. The liver was slightly enlarged, the spleen was not felt. The urine was small in amount and contained albumen. The temperature during his stay in hospital was generally sub-normal, but on one or two occasions it rose to 100 degrees Fahr.. A

blood cultivation was not made. During his stay in hospital he was on three occasions treated with digitalis without material benefit, and on each occasion it had to be stopped on account of sickness. He died on May the 12th, 1912.

*The polygraphic tracings.*

Numerous polygraphic tracings were taken throughout the patient's stay in hospital. The *a-c* interval was constantly increased, and on each of the three occasions on which digitalis was administered, incomplete heart

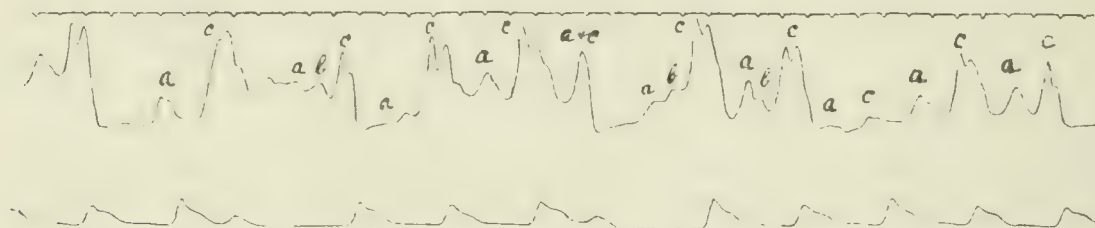


Fig. 1. Normal rhythm with long *a-c* interval, many of the *a* waves show a tendency to a division into two separate waves. This tendency is unaltered in *a* waves succeeding the compensatory pauses of the extrasystoles. Upper tracing jugular, lower radial, time-marker one-fifth of a second.

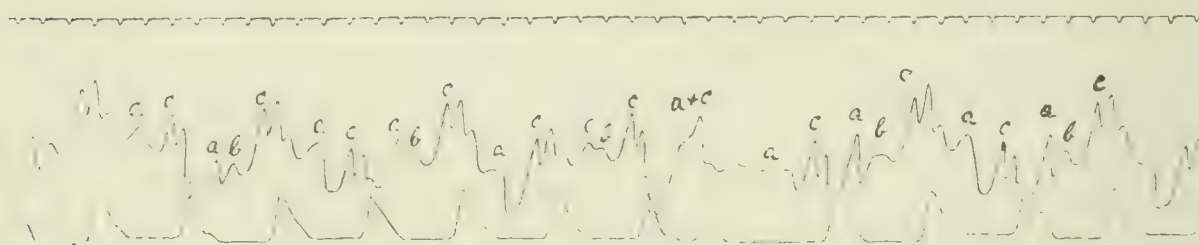


Fig. 2. Normal rhythm; long *a-c* interval; conspicuous *b* wave between *a* and *c*.

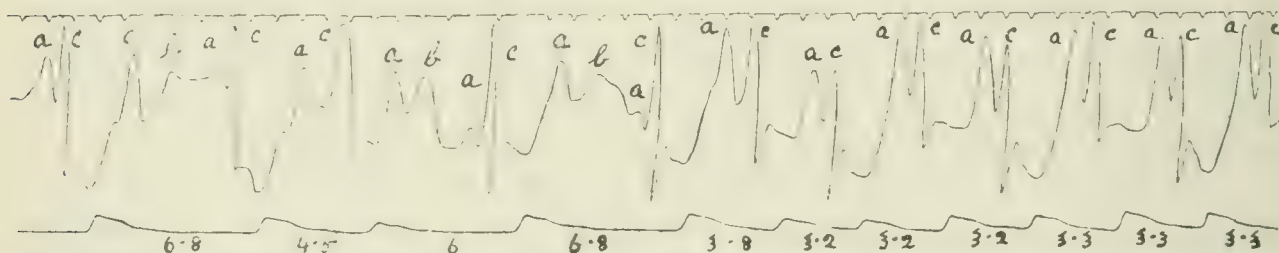


Fig. 3. Incomplete block after digitalis. Conspicuous *b* wave following the blocked auricular systoles.

block occurred after about 10 drachms of the drug had been taken. Frequent extrasystoles were invariably present; they will be described later in more detail.

Fig. 1 is a tracing taken on March the 4th, and shows an *a-c* interval of fully three-tenths of a second in length. Most of the *a* waves show a distinct tendency to a division into two separate waves. This differentiation into two quite separate waves was frequently present throughout long strips of tracing. An example is shown in Fig. 2, and it raises the question whether the first presystolic wave and the apparent lengthening of the *a-c*



interval is not due to the fusion of a *b* wave with the first part of the *a* wave. That this is not so is shown by the persistence of the double wave in the same position in the cycles succeeding the compensatory pauses of the premature contractions. A similar double *a* wave accompanies the blocked auricular systoles during the periods of incomplete block produced by digitalis, and here again it is evident from Fig. 3 that the first of the waves must be regarded as the true auricular wave.

A similar curve showing the presence of two clear presystolic waves has been described by Laslett and he points out that a curve published by Cowan<sup>1</sup> and Ritchie is probably of the same nature. In Laslett's<sup>3</sup> case a true *b* wave could be excluded, as the relation of the two peaks to each other remained unchanged under very varying cardiac rates. He considers that both waves are auricular in origin, and are an expression of hypertrophy of the right auricle, but he makes no further suggestion as to the mechanism of the second wave. In the present case, the right auricle was distinctly dilated and not hypertrophied. Griffith and Cohn<sup>2</sup> have also recorded a very similar curve from a case presenting a long *a-c* interval. Many of the tracings showed a well marked wave (*b*<sup>1</sup>) occurring between the *a* and *c* waves or obscuring the beginning of the *c* waves. As in the present case, when an auricular contraction was not followed by a ventricular systole in consequence of a blocking of the stimulus, this post-auricular wave appeared unchanged. It is evident from Fig. 3 that if the second peak of the *a* wave is to be attributed to a direct contraction of the auricle, the auricle must have remained in systole for almost .4 of a second. Griffith and Cohn, with whom we agree, consider the second wave to be essentially the same as the diastolic wave of Gibson and Hirschfelder and due to the temporary closure of the tricuspid valves consequent on the rush of blood into the ventricle following the auricular systole, and probably accentuated by incompetence of the valve.

Fig. 4 taken on March the 14th after the patient had had 10 drachms of tincture of digitalis, shows a condition of incomplete heart-block with mixed responses. Fig. 3 taken on the same date also shows incomplete heart-block. Three days after the digitalis was stopped the heart-block disappeared and the heart reverted to the former rhythm with a long *a-c* interval. An exactly similar condition appeared on the two later occasions on which digitalis was given, in each instance after the administration of 10-12 drachms of the tincture.

On every occasion on which the heart was examined during the periods when heart-block was absent, extrasystoles were numerous. These were most frequently as single beats, but occasionally two or three occurred in succession, and more rarely short paroxysms of five or six. The pauses following single extrasystoles were always fully compensatory and throughout the whole of the patient's stay in hospital, whenever groups of two or more extrasystoles occurred in succession, the post-paroxysmal pause in the radial pulse was invariably almost exactly equal to the compensatory pause

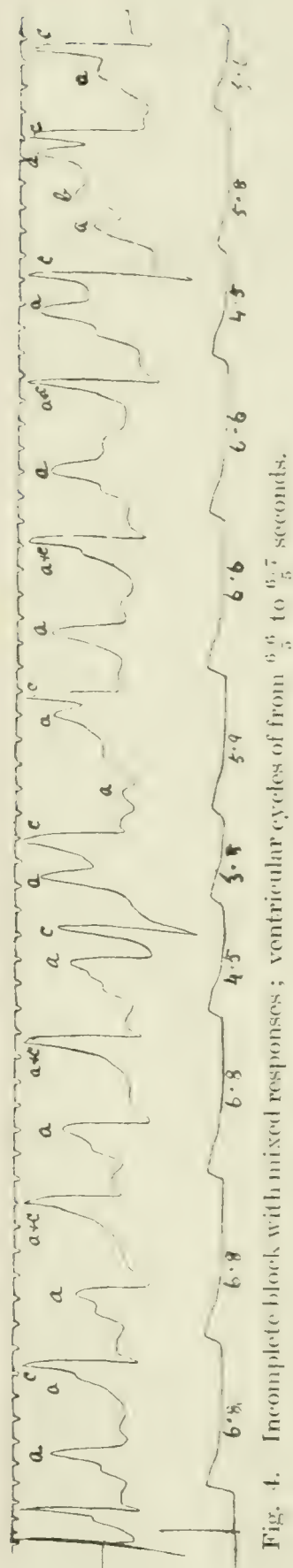


Fig. 4. Incomplete block with mixed responses; ventricular cycles of from  $6\frac{6}{5}$  to  $6\frac{7}{5}$  seconds.

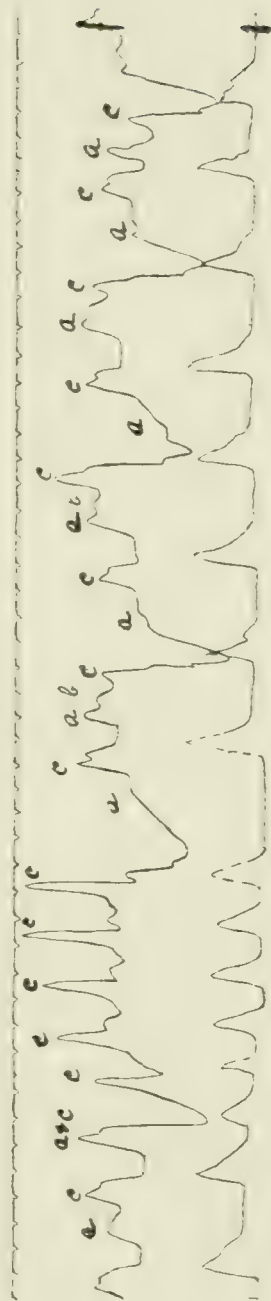


Fig. 5. Short paroxysm of tachycardia. The post-paroxysmal pause is exactly equal to the pause in Fig. 6, and the compensatory pauses in Fig. 1 and 2. The venous pulse is of the ventricular type.

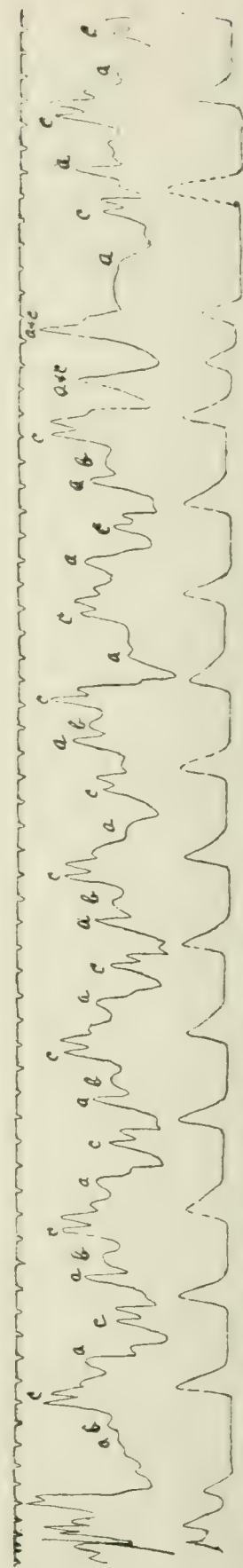


Fig. 6. Two successive extrasystoles; ventricular type of venous pulse with disturbance of auricular rhythm.



of the single premature contractions. Owing to the difficulty of exactly determining the commencement of the *a* wave in the phlebogram, both during and immediately after the premature contraction, it is impossible to determine the exact length of the pause in the jugular. Fig. 1 and 2 show the occurrence of single premature contractions with fully compensatory pauses. The *a* and *c* waves occur simultaneously and so far as one can measure the *a* wave is not premature. Taken by themselves these premature contractions might be ventricular in origin or might arise in the junctional tissues.

Fig. 6 shows the occurrence of two successive extrasystoles and Fig. 5 a short paroxysm of six beats. In both, the post-paroxysmal pause in the radial pulse is equal to the compensatory pause of the single extrasystoles and, in both, there is a disturbance of the auricular rhythm. The venous pulse during the paroxysm is of the ventricular type and the height and general character of the waves strongly suggest that they are due to a simultaneous contraction of the auricles and ventricles. Such a condition may arise in one of three ways. As a result of an increase in the *a-c* interval the *a* wave may fall back on the *c* wave of the preceding cycle: a similar venous tracing may be produced by a ventricular tachycardia retrograde to the auricle, or the condition may result from a true nodal rhythm. In the present case, the complete absence, at any time, of single premature contractions arising in the auricles and the fact that the post-paroxysmal pause in the radial is exactly equal to the compensatory pause of the single premature contractions, which manifestly do not arise in the auricle, is sufficient to exclude the auricular origin of the short paroxysms. Retrograde extrasystoles are extremely unlikely in the presence of a long *a-c* interval, and although there is a shoulder to the descending limb of the second extrasystole in Fig. 6 which might suggest a retrograde *a* wave, the interval between it and the succeeding *a* wave of the normal rhythm is less than a normal auricular period. The origin of the paroxysms must therefore be attributed to the junctional tissues, and as the compensatory pause in all the single and successive extrasystoles is exactly equal it is probable that all the premature contractions in this case arose from a single focus in the junctional tissues.

Alternation of the pulse after a single extrasystole is shown in Fig. 1.

#### *Autopsy.*

The spleen was much enlarged and showed numerous infarcts.

The heart weighed 19 oz..

The pericardial sac contained  $4\frac{1}{2}$  oz. of clear serous fluid. The pericardium was smooth and glistening.

In situ the greatest longitudinal diameter was 6 inches. The greatest transverse diameter  $5\frac{1}{2}$  inches. All the cardiac chambers were relaxed and contained a moderate amount of blood.

Over the inter-ventricular septum there was a slight elevation which on palpation suggested the presence of several distinct nodules in the heart muscle. On incision, however, no definite macroscopical lesion could be seen and after fixation with 8 per cent. formalin in normal salt solution, these nodules could no longer be differentiated from the rest of the cardiac muscle. The aortic valve measured .85 inch in diameter and was incompetent when filled with water. The mitral valve measured 1.7 inches. The tricuspid ring admitted four fingers. After fixation, the left ventricle measured  $3\frac{3}{4}$  inches and the thickness of the wall varied from  $\frac{1}{2}$  to  $\frac{3}{4}$  inch.

All three aortic cusps had enormous pale yellow vegetations attached to them. Some of these arched upwards and backwards over the concavities of the sinuses of Valsalva, the posterior extremity of the arches becoming adherent to the wall of the aorta. The right posterior cusp was almost completely destroyed. The openings of the coronary arteries were patent and normal. Below the aortic valves, occupying almost the whole area of the membranous septum and extending for a short distance on to the base of the anterior mitral cusp was an oval ulcerated patch the floor of which was covered with nodular vegetations. The patch measured 1 inch by  $\frac{7}{16}$  inch. Below the ulcerated area there were a few small vegetations about the size of a millet seed.

The free margins of the mitral valve were normal, but there were a few small vegetations on the *chordæ tendineæ*. The rest of the endocardium was slightly milky and opaque.

The left auricle was slightly dilated and its wall measured one-sixteenth of an inch in thickness.

The right ventricle measured  $4\frac{1}{4}$  inches, the thickness of the wall averaged a quarter of an inch. The tricuspid orifice was dilated, but the cusps were normal. The pulmonary cusps were normal. The right auricle was dilated and its wall distinctly thin.

For microscopic study blocks of tissue were taken from the heart as follows :—

1. The *a-v* junction containing the *a-v* node and the whole of the membranous septum.
2. The region of the sino-auricular node.
3. Several portions of the inter-ventricular septum and of the right and left ventricles.
4. Portions of the right and left auricles.
5. Portions of the right and left muscoli papillares.

1. *The a-v bundle.* The usual block was embedded in paraffin and cut in serial sections 10 micra in thickness, at right angles to the long axis of the block. Every tenth section was kept and stained with hæmatoxylin and eosin.



The ulcerated patch, seen macroscopically on the membranous septum, presented the usual appearances of an ulcerating endocarditis.

The inflammatory process in the anterior part of the membranous septum extended practically throughout the whole thickness of the septum which was freely infiltrated with cells. These consisted of polymorphonuclear leucocytes, lymphocytes and plasma cells. In some of the granulations a few giant cells of the type met with in rheumatic infections, were found. Fig. 10 is a photograph of such a cell. In sections stained by the Gram-Weigert method, numerous cocci, many of which had the diplococcal form, were seen. In the posterior part of the membranous septum the inflammatory changes only extended throughout the whole thickness of the septum in its upper half.

Tracing the *a-v* bundle from below upwards, in its course through the membranous septum, it was found to be intact and free from all abnormal cellular infiltration at its lower part. As it passed upwards it gradually became more and more infiltrated with round cells which were in parts diffuse, and in parts arranged in dense foci in the vicinity of the vessels. Most of these cells appeared to be lymphocytes. The vessels were dilated and engorged. Fig. 8 and 9 are from this region. The cellular infiltration and the dilatation of the vessels considerably encroached upon and widely separated the muscle fibres of the bundle. Further backwards the inflammatory changes again diminished, and apart from slight perivascular infiltration the first portion of the main stem and the *a-v* node appeared normal.

2. *The sino-auricular node.* The sino-auricular node was cut in serial sections. It was well developed. Apart from an unusual prominence of the smaller blood vessels, and the presence of very slight cellular accumulations around one or two of the capillaries in the periphery of the node, it was normal.

3. *Portions of the inter-ventricular septum and of the right and left ventricles.* Blocks of tissue containing part of the interventricular septum, and those portions of the right and left ventricles from the areas which appeared indurated and nodular at the autopsy, were embedded in paraffin, cut and stained with hæmatoxylin and eosin. In the pericardium there was congestion of the vessels with slight perivascular accumulation of small round cells, consisting for the most part of lymphocytes and plasma cells. The muscle tissue of the ventricles showed conspicuous engorgement of the vessels, and here and there very small perivascular accumulations of cells, mostly lymphocytes, but the changes on the whole were very slight. Immediately below the endocardium in two of the *columnæ carneæ*, there were small necrotic areas about the size of pins' heads, in which the muscle fibres had lost their staining reactions and the nuclei had disappeared. There was no cellular infiltration. The necrotic areas were sharply demarcated from the normal muscle and appeared to be minute infarcts.

Other regions of the ventricle showed vascular dilatation and engorgement, and here and there very slight perivascular cell accumulation. Stained with Scharlach R., frozen sections showed a few minute globules of fat round the nuclei of the muscle fibres.

4. Portions of the right and left auricles showed similar changes to those in the ventricles, but they were less conspicuous.

5. The musculi papillares were in a similar condition to the rest of the ventricular muscle.

We are much indebted to Dr. Duncan for the micro-photographs.

#### SUMMARY.

A case presenting a long *a-c* interval, associated with short paroxysms of tachycardia originating in the junctional tissues, is reported.

Post-mortem an acute inflammatory lesion was discovered beneath the aortic valves. It involved the middle third of the main stem of the *a-v* bundle.

#### REFERENCES.

- <sup>1</sup> COWAN AND RITCHIE. Quart. Journ. Med., 1910-11, IV, 66.
- <sup>2</sup> GRIFFITH AND COHN. Quart. Journ. Med., 1909-10, III, 126.
- <sup>3</sup> LASLETT. Quart. Journ. Med., 1911-12, V, 377.



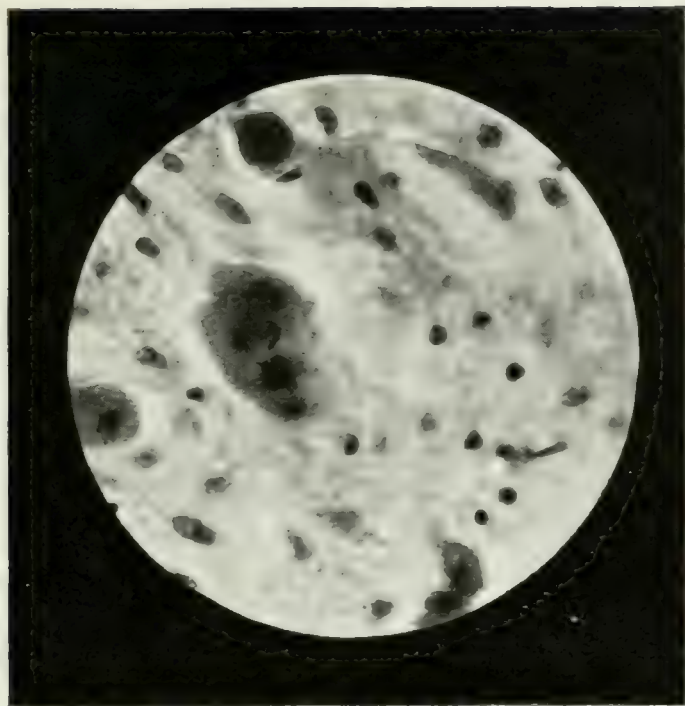


Fig. 10.

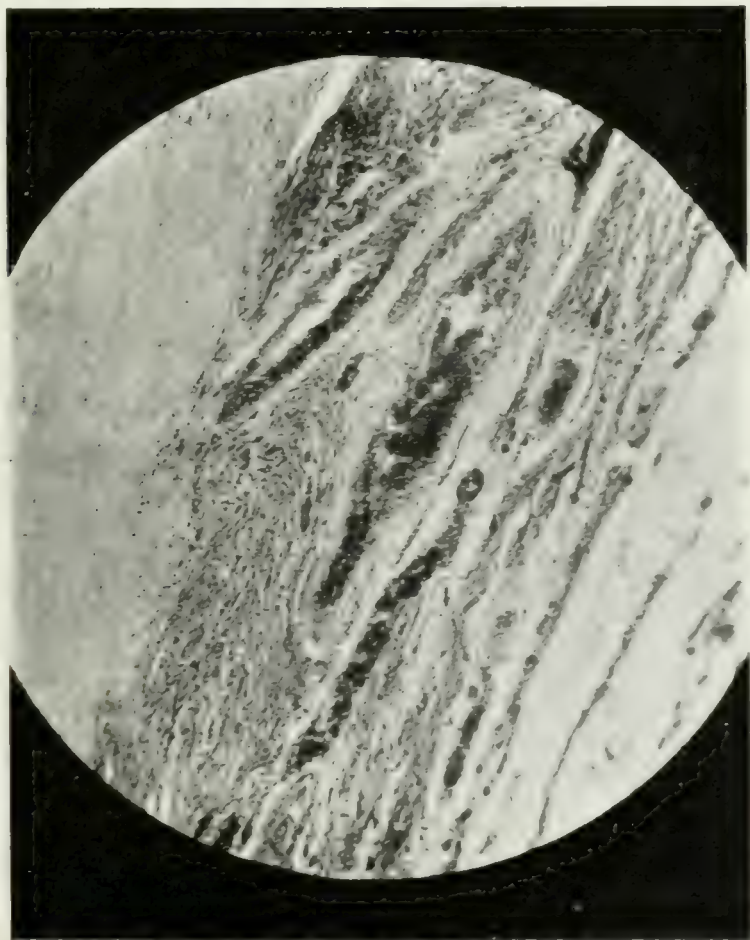
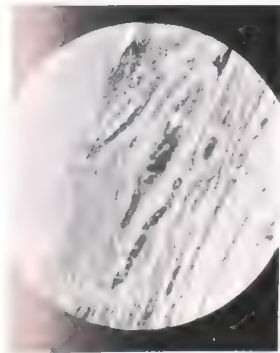
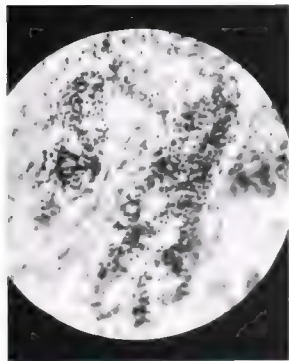
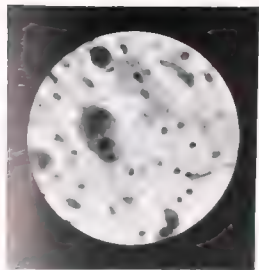
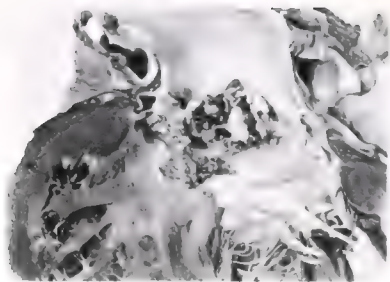


FIG 9.





## ON SIMULTANEOUS RECORDS OF THE HEART SOUNDS AND THE ELECTROCARDIOGRAM.

By GEORGE FAHR.

*(From the Physiological Laboratory of the University of Leyden).*

It is apparent that we can obtain valuable information as to the time relations of the various phenomena of a cardiac cycle from simultaneous records of the electrocardiogram and the heart sounds. In the first place it is possible to determine the moment when the heart sounds first appear over the different regions used in auscultating, by referring the beginning of the heart sounds recorded in these regions to a given point in the electrocardiogram. In the second place we can determine the time relations of a given peak of the electrocardiogram in the three different leads by referring it in each lead to a given point of the phonocardiogram. In making these determinations we assume that the various points of the electrocardiogram and the phonocardiogram always fall in exactly the same phase of the heart beat. And in the third place we can determine the relations between the phases of the heart beat and the peaks of the electrocardiogram, if we assume that the phase of the heart beat is known in which the heart sounds begin.

The recording of the electrocardiogram can only be done successfully at present with the string galvanometer according to the method introduced by Einthoven. On the other hand there are several methods at present for the recording of the sounds of the heart. Reference may here be made to the mechano-optical methods of Frank,<sup>6 & 7</sup> Weiss,<sup>20 & 21</sup> Gerhartz,<sup>8 & 9</sup> and Hürthle,<sup>11</sup> and to the electro-optical method with the string galvanometer first applied by Einthoven.<sup>2</sup> Bull<sup>1</sup> has cleverly arranged the string galvanometer and the phonoscope of Weiss so as to record the electrocardiogram and the phonocardiogram above one another on the same photographic plate. A very good way would be to record the excursions of two string galvanometers upon the same plate, the one galvanometer recording the electrocardiogram and the other the heart sounds.

As most investigators must content themselves with the use of one string galvanometer, the method of recording the electrocardiogram and the heart sounds simultaneously with one string comes strongly into consideration because of the ease in carrying it out. The first results obtained with this method have been published by Kahn.<sup>13</sup> He has mainly studied the time relations between the different phases of the heart beat and the points of the electrocardiogram, under the assumptions that the beginning of the first heart sound coincides with the beginning of ventricular contraction, and that the second sound coincides with the commencement of diastole. As far

as our work has repeated that of Kahn, it is in essential agreement with his results. But our paper will deal especially with the time relations of the peaks of the electrocardiograms as obtained by the various leads, and with differences in the time of commencement of the first heart sound near the apex beat and in the second intercostal spaces on each side of and close to the sternum.

In order to get an exact record of sound waves with the string galvanometer, it is necessary to increase the tension of the string until the deflection time of the string is at least twice as small as the period of the sound waves to be recorded. In our work the tension on the string was such that the sensitiveness of the galvanometer was a quarter that usually used in electrocardiographic work. Under these circumstances the string was quick enough to record the heart sounds with the desired accuracy, and the peaks of the electrocardiogram, though reduced a quarter, were still easily recognizable. The resistance of the secondary coil of the transformer as well as the resistance of the body were always in the circuit when adjusting the sensitiveness of the string, so that 1 mm. along the ordinates represents  $4 \times 10^{-4}$  volts. It is worthy of mention that under these circumstances the movements of the string were still aperiodic and the deflection time about 0.005 sec..

The speed of the photographic plate was about 100 mm. per sec., so that 1 mm. along the abscissæ represents about 0.01 sec.. The movement of the spoked wheel is so uniform and exact that the shadows represent 0.01 sec., with no greater error than 0.0001 sec.. The negatives were measured under a microscope with the aid of a mechanical stage and an ocular with cross hairs. With this arrangement we could measure distances with 0.05 mm. accuracy, or the time with an accuracy of 0.0005 sec..

Although the measuring instruments allowed of this great accuracy, it was impossible to measure the time between any given peak of the electrocardiogram and the commencement of the first heart sound with the same exactness, because of the impossibility of determining the commencement of the sound as exactly in the simultaneously recorded phono- and electrocardiogram. The commencement of the first sound lies in either the ascending or descending branch of peak *R* and is not sharply marked. For this reason it is only possible accurately to set the cross hairs of the ocular upon one of the sharper peaks of the heart sound curve. This makes it necessary to calculate the distance from a given peak of the electrocardiogram to the beginning of the first heart sound from measurements made upon two plates. These two plates are the simultaneous phono-electrocardiogram and the phonocardiogram alone. The distance from the commencement of the heart sound to an easily recognizable peak of this sound was first determined in the plate containing the phonocardiogram alone, and then the distance from the given peak of the electrocardiogram to this easily recognizable peak of the heart sound was measured in the simultaneous curve. From these two measurements the distance from the commencement of the sound to the peak of the electrocardiogram was calculated.



A record of the electrocardiogram alone under exactly the same conditions was always made upon a third plate. By means of measurements upon this plate and the first mentioned measurements it was possible to calculate the distance from any point of the electrocardiogram to the commencement of the first sound. The sharp peak *R* of the electrocardiogram was used wherever possible for that point of the electrocardiogram from which the measurement to the easily recognizable peak of the heart sound was made, because only this peak of the electrocardiogram can be determined with an accuracy of 0.0005 or 0.001 sec.. The other electrocardiographic peaks are not sharp enough. But in many cases the beginning of the first sound lies in the anacrotic limb of *R*, and the summit of *R* is then uncertain because of the superposed sound vibrations. In such cases we made use of the commencement of the ventricular electrocardiogram for the starting point of the measurement. This point is not so sharp as the summit of *R* and there is consequently no greater accuracy than 0.001 or 0.002 sec. in these measurements. We repeated our measurements upon positives made from the original negatives. In this series of determinations we measured the distances from the commencement of the ventricular electrocardiogram to an easily recognizable peak of the first heart sound upon the phono-electrocardiogram and calculated the other distances from measurements made on the positives of the corresponding electrocardiograms and phonocardiograms alone. Professor Einthoven was kind enough to control these measurements and there was never a difference of more than 0.001 sec. between the measurements made by him and those made by us.

Slight changes in the form of the sound waves are a source of error which it is impossible to avoid. From one first sound to the next following first sound the distance between any two vibrations of the curve of the first sound never varies more than 0.0005 sec., but in the course of a few minutes this distance often changes as much as 0.001-0.002 sec.. There was an interval of about two minutes between the recording of the phono-electrocardiogram and the recording of the phonocardiogram. Thus an error of 0.001-0.002 sec. in the determination of the time interval from a given peak to the commencement of the first sound is possible from this source. No measurements were made where the change in the form of the sound wave could be seen easily with the naked eye.

Another source of uncertainty in the measurements is the variable form and length of the initial vibrations of the first sound. The first sound begins with one or more vibrations of longer period than the rest of the sound. These first vibrations are also of much smaller amplitude, and the form is often quite variable in the same person, often even from one heart beat to the other. We shall return to these vibrations later. Suffice it to say that we used the mean between measurements made on two or more phonocardiograms when determining the time from the beginning of the first heart sound to an easily recognizable peak of this sound, because this distance varies with the variations in the form of the initial vibrations of the first

sound. It was impossible to make use of the second heart sound in calculating the time interval between a given peak of the electrocardiogram by different leads, despite the more constant character of this sound, because the variations in the length of systole sometimes amount to 0.005 or 0.01 sec. from heart beat to heart beat.

Despite these sources of error, the agreement between the values obtained from measurements upon a series of phono-electrocardiograms, taken from the same person during the same sitting, is quite good. It was impossible to measure more than two or three phono-electrocardiograms on one photographic plate and we never took more than two plates in succession; thus we never had more than six measurements, often only two or three, from which to calculate a mean value. The number of the measurements is therefore too small for the calculation of an exact value of the probable error according to the method of least squares. We have calculated the mean of the differences of the individual measurements from the mean value of the measurement and in only two cases was this value greater than 0.003 sec.. In the majority of cases the mean variation from the mean value was not larger than 0.001 sec..

There are two other factors that must be taken into account, namely, the time taken in the transmission of the sound from the walls of the chest to the microphone and perhaps the lag of the current in the apparatus for transmission. We obtained a correction figure for both of these factors together by determining the latent time between the making of an electrical contact and the beginning of the curve of the sound produced by the making of the contact. A falling hammer actuated by an electro-magnet made contact with a metallic contact piece placed close to the stethoscope opening. The contact closed the circuit of a signal<sup>2</sup> whose latent time is 0.0001 sec.. At the moment of making contact a sound was produced by the metallic pieces and this sound was carried to the microphone and recorded under precisely the same circumstances as the heart sounds. The latent time thus determined was 0.0025 sec.. All the values in our tables have been corrected for this. As the velocity of sound in tubes of the diameter (2 cm.) used in our work will only be about 0.2 per cent. less than in the open air<sup>15</sup> we can take a velocity of 330 metres for the velocity of sound in the rubber tubing leading from the stethoscope to the microphone. The length of the rubber tubing was 72 cm., and the time necessary for the transmission of the sound from the stethoscope to the microphone was 0.0022 sec., so that we can calculate a lag of the current of 0.0003 sec., an altogether negligible quantity.

We only made use of the second heart sound when determining the interval between the end of peak *T* and the commencement of the second sound. It was impossible to get a good measurement of this interval directly, because the curve of the phono-electrocardiogram shows slight waves along the descending branch of *T*. These waves, due to an unsteadiness in the phonocardiogram during the period following the first sound and preceding the second sound, make it impossible to determine exactly where



the peak *T* ends. For this reason we found it better in the majority of cases to determine the value of the interval from the end of *T* to the beginning of the second sound from measurements on three different curves, namely electrocardiogram, phonocardiogram, and phono-electrocardiogram. The interval from the summit of *T* to the end of *T* was measured on the electrocardiogram, the interval from the commencement of the second sound to an easily recognizable peak of the second sound curve was measured on the phonocardiogram, and finally the interval from the summit of *T* to the easily recognizable peak of the second heart sound curve was measured on the phono-electrocardiogram. From these measurements the time interval from the end of *T* to the commencement of the second sound was calculated. The duration of systole as measured from the beginning of the first sound to the beginning of the second sound can vary 0.01 sec., though we find that in most cases it does not vary more than 0.002-0.003 sec.. For this reason we did not use the second sound for any other calculations, and in using it to find the time interval from the end of *T* to the beginning of the second sound we are conscious of the fact that the values so obtained may have no greater accuracy than about 0.01 sec.. At the same time we believe that our values give the direction and the order of magnitude of the interval from the end of *T* to the commencement of the second sound very well. We have the more reason to believe this because we have some records of phono-electrocardiograms in which it is possible to determine the interval directly from one curve, because the string was perfectly quiet along the descending branch of *T*; and the directly determined values agree with the indirectly determined values for the same individual.

We fixed the stethoscope upon the thorax at a point 1.2 cm. inside the mamillary line, when taking the heart sounds over the apex. The apex beat in all the individuals investigated by us was hardly perceptible in the supine position used; and, as the tube leading from stethoscope to microphone had an opening in it, there is little probability that the apex beat caused a deformation of the heart sound curves.<sup>2&5</sup> The heart sounds over the aortic and pulmonary valves were taken in the second intercostal spaces to right and left of the sternum, respectively. In general we first recorded the electrocardiogram with a sensitiveness of four millivolts equal to one centimetre, and then, after an interval of two minutes, which was necessary for changing the photographic plate, the phono-electrocardiogram would be recorded, and after another two minutes the phonocardiogram. Then followed another phono-electrocardiogram. These four plates taken with lead *I* would then be followed by the recording of four similar plates with leads *II* and *III*, respectively.

In order to make these records of electrocardiogram, phonocardiogram, and phono-electrocardiogram quickly and easily, we made use of the connections shown schematically in Fig. 1. The non-polarisable electrodes *E*, the transformer *SP*, and the microphone *M* were set up in a room which was kept as quiet as possible because all accidental sounds influence the microphone.

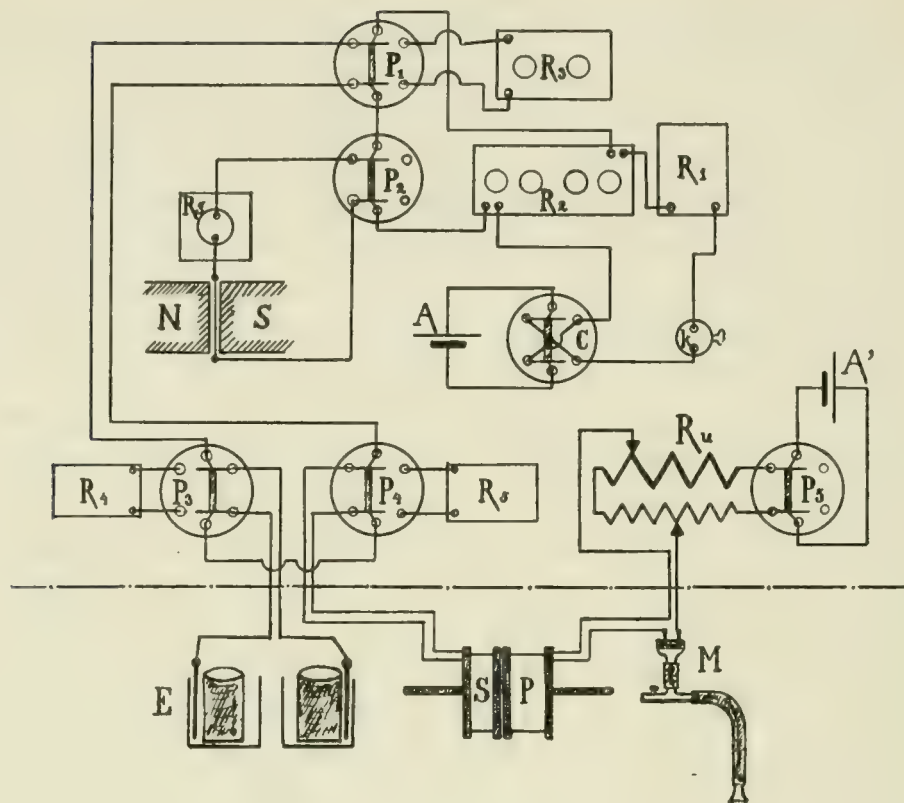


Fig. 1.

The wires from the electrodes  $E$ , from the secondary coil  $S$ , from the primary  $P$ , and from the microphone  $M$  were carried in cables from this room into the galvanometer room where the rest of the arrangement was set up. The accumulator  $A'$  furnished the current for the circuit of the microphone and the primary coil. The intensity of this current was regulated by means of the sliding resistance  $R_u$ , while the opening and closing of the circuit was made with the aid of the key  $P_5$ . In taking the phono-electrocardiogram the body and the secondary coil of the transformer are in the circuit of the galvanometer, and it is necessary that an equivalent resistance be substituted for that which may not be in the galvanometer circuit when recording the phonocardiogram or the electrocardiogram alone, if the conditions are to remain the same. By means of the switch  $P_4$  we could substitute the equivalent resistance  $R_5$  for the secondary coil when taking the electrocardiogram alone. And in the same way the switch  $P_3$  provided a means of substituting the equivalent resistance  $R_4$  for the body when taking the phonocardiogram alone. The resistance of the body for each lead was always determined first and then  $R_4$  was made equal to this resistance. The wires leading from the switches  $P_4$  and  $P_3$  to the switch  $P_1$  carried the current from  $E$  or  $S$  or from both together, as the case might be, through the switch  $P_1$  into the arrangement ordinarily used in the Leyden laboratory for recording the electrocardiogram. We have also included this latter arrangement in the schema.



Before proceeding to the results of our measurements we wish to describe a peculiarity of the first sound which will later be noticed as an explanation of the differences in the values found for different persons, as well as for the explanation of the differences found in the values of the time intervals for the same person on different days. For the construction of the tables we have only used the results of experiments made as fast as possible one after the other on the same day, because otherwise changes in the form of the sound waves would cause errors in the calculations. We sometimes found conspicuous changes in the form of the sounds taken on different days. As an example of this we refer to the heart sounds of de W. Fig. 2 taken on June the 6th, 1910, and Fig. 3 taken on July the 8th, 1910. Both records

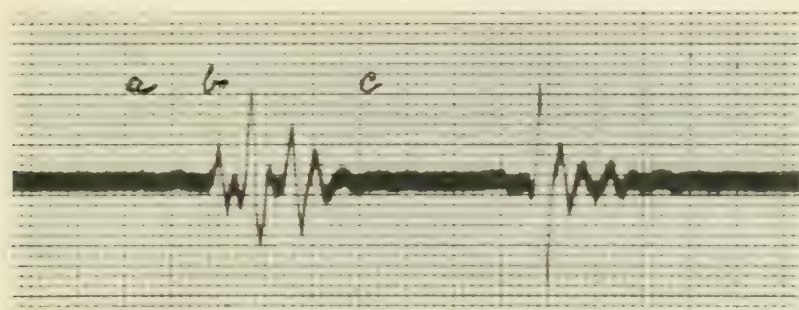


Fig. 2. Phonocardiogram of de W.. June the 6th. Stethoscope in fifth intercostal space, 1 cm. inside mam. line. *ab* are the initial vibrations which are here so small that they would not be recognized if the string was not perfectly quiet during diastole. In this as in all the figs. excepting 11 and 12, 1 sec. div. Absc. = 0.01 sec., and 1 sec. div. Ordin. =  $4 \times 10^{-4}$  volts.

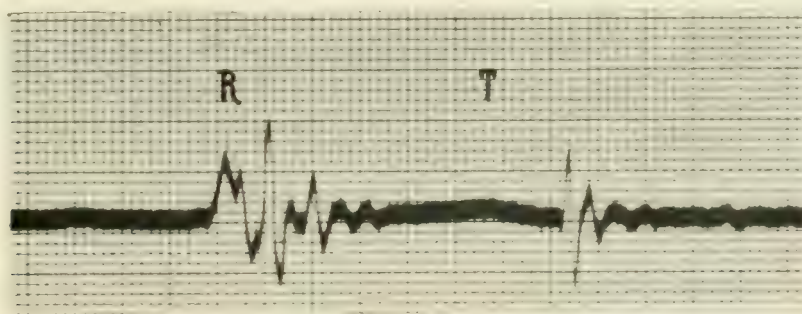


Fig. 3. Phono-electrocardiogram of de W.. Lead II. Taken immediately after Fig. 2.

were made under the same conditions, as far as we could control them, the stethoscope being fixed in both cases upon the thorax in the fifth intercostal space 1 cm. inside the mamillary line. The part *ab* of Fig. 4 consists of vibrations whose period is longer and whose amplitude is smaller than the vibrations of the part *bc*. We shall hereafter call the part *ab* the initial vibrations and the part *bc* the main vibrations. The part *ab* corresponds to the "Vorton" of German authors. If we examine Fig. 2 we see that it also has the initial vibrations but they are here so small that they can only

be made out upon close inspection, whereas the initial vibrations of Fig. 4 are very prominent. If we had used a little less current in the microphone circuit while recording Fig. 2, the two initial vibrations would have been too small to recognize. Or if the string had not been perfectly still during the period following the end of the second sound and preceding the first sound, then the two initial vibrations of Fig. 2 would not have been distinguishable from the accidental vibrations. It is not often that one gets records of heart sounds so free from accidental vibrations as Fig. 2, and in many cases initial vibrations must be present where they are not to be distinguished because of

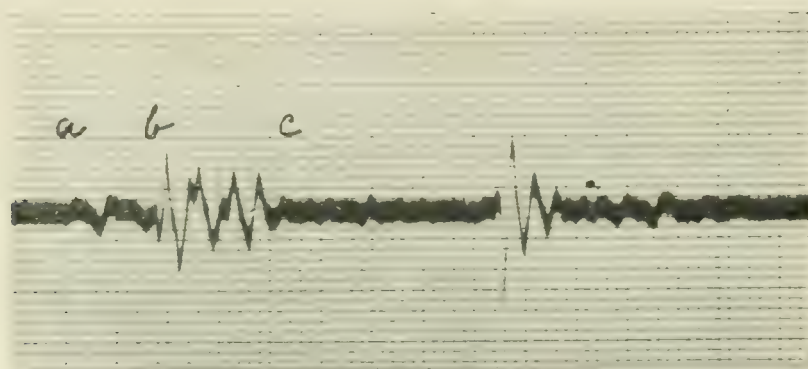


Fig. 4. Phonocardiogram of de W., July the 8th. Stethoscope in fifth intercostal space 1 cm. inside mam. line. *ab* are the initial vibrations here especially well developed.

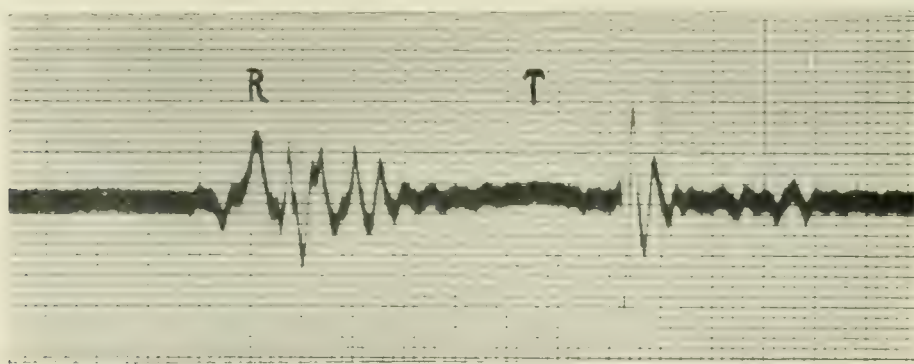


Fig. 5. Phono-electrocardiogram corresponding to Fig. 4. Taken immediately after Fig. 4. Lead II.

the accidental vibrations. It appears to us that this uncertainty in making out the initial vibrations of the first heart sound is the cause of the variations in the values for the time interval from the summit of *R* to the commencement of the first sound in the same individual on different days. As another example of this we refer to the apex sounds of Fa. (Fig. 9) recorded on June the 7th, 1910, where relatively large initial vibrations (*ab*) are to be seen. A calculation from measurements made in this curve and in Fig. 10, taken shortly after Fig. 9, shows that the apex sound appears 0.017 sec. before the summit of *R*; whereas a calculation from records of the same person, taken under the same circumstances on July the 11th, 1910, gives the first sound



as coming 0.025 sec. after the summit of *R*. In this latter case, the records of which we shall not publish here, no initial vibrations could be made out with certainty, because the string was not free from small vibrations during the period following the second sound. In many cases where the initial vibrations are to be seen in the records of the sounds taken over the apex, they are also to be made out in the records of the sounds taken over the aortic and pulmonary valves; but in general the initial vibrations cannot be made out in the sounds recorded from the region of the arterial valves, because it is necessary to use a stronger current in the microphone circuit in recording these sounds and the height of the accidental vibrations is increased with the increase in current. If we could use stronger currents in the microphone circuit, without increasing the accidental vibrations, not only would it be possible to show the initial vibrations of the first apex sound with certainty, but they would undoubtedly always be found over the aortic and pulmonary valves too. As the differences in the values of the time interval, from the summit of *R* to the commencement of the first sound, in the same person and on different days, are at least as large as those between different persons, we wish to ascribe this difference at least partly to the presence or absence of the initial vibrations in the curve of the first heart sound. Before we leave this subject for the present we wish to refer to the one published record of Bull<sup>1</sup> where the initial vibrations are to be seen also.

At present we cannot give an explanation of these initial vibrations, which is founded upon experiments; but we consider the explanation of Hürthle<sup>12</sup> and Weiss,<sup>21</sup> that the initial vibrations ("Vorton") represent the sound of the contracting auricle, as untenable. We are in possession of over fifty phono-electrocardiograms, in which the sounds were taken from the region of the apex and which were recorded from seven persons at different times. With the exception of the case of de W., on one day, the commencement of the initial vibrations in all these records lies in the ascending branch of *R*, and the initial vibrations are continuous with the rest of the first sound without pause. The auricular peak *P* of the electrocardiogram begins about 0.12-0.18, sometimes nearly 0.2 sec., before the commencement of the ventricular electrocardiogram, and has a duration of about 0.07-0.08 sec.; so that a pause of about 0.05-0.1 sec. intervenes between the auricular and the ventricular electrocardiogram. From this fact we conclude that an auricular sound would begin about 0.12-0.18 sec. before the ventricular sound. In all our cases, excepting the one of de W., on July the 8th, the initial vibrations began much later, namely, only about 0.02-0.04 sec. before the main vibrations. Another argument against the acceptance of the initial vibrations as the sound of the contracting auricle is found in the results of experiments upon the intraventricular pressure. In the classical researches of Marey and Chauveau<sup>16</sup> we see the same interval of time between the beginning of the auricular and the beginning of ventricular contraction as in the electrocardiogram.

It appears more probable to us that the initial vibrations of the first sound are connected with the activity of the ventricles, and especially with the contraction of the ventricles during the period of tension before the opening of the semilunar valves. According to this conception they would correspond in time with the "Vorschwingungen" described by Frank<sup>7</sup> in the pulse of the aorta, and interpreted by him as the expression of the rise in pressure in the ventricle during the period of tension and before the opening of the semilunar valves. In a woman investigated by Tigerstedt<sup>19</sup> the period of tension was 0.05 sec.. We find the duration of the initial vibrations to be 0.02-0.04 sec., with the exception of the case of de W. where the duration of the initial vibrations was 0.09-0.10 sec. on the one day. Einthoven and Geluk<sup>5</sup> have published a case where the sound over the apex precedes the first sound over the arterial valves by 0.06 sec.. The initial vibrations in the one published record of Bull<sup>1</sup> come about 0.05-0.06 sec. before the main vibrations.

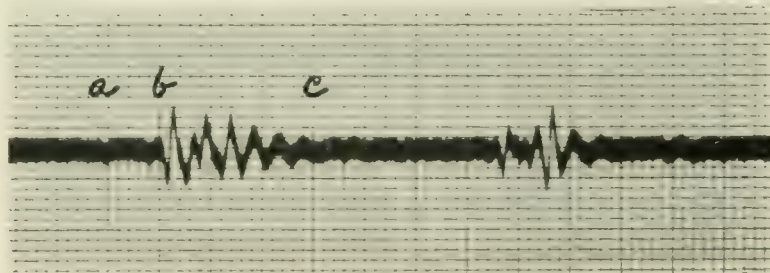


Fig. 6. Heart sounds of de W., July the 8th. Recorded in second intercostal space left of sternum, immediately after Fig. 7. By careful inspection two waves can be made out which correspond to the two deeper waves of the initial vibrations of Fig. 4 in all probability.

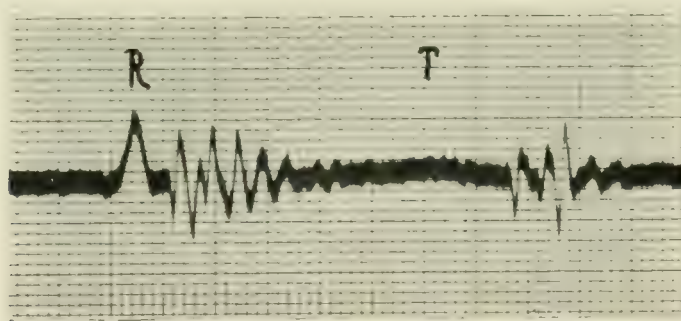


Fig. 7. Phono-electrocardiogram of de W., corresponding to Fig. 6. Lead II. Taken immediately before Fig. 6. The two small vibrations of Fig. 6 are here also to be made out. They come before the beginning of R just at the point where the corresponding deeper waves of the initial vibrations of Fig. 4 are seen coming before R in Fig. 5.

The initial vibrations are relatively much larger in the sounds taken over the apex than in the sounds recorded over the aortic and pulmonary valves, and this suggests that the differences in time of commencement of the first sound over the apex and over the arterial valves is to be explained by the apparent absence of the initial vibrations over the second intercostal space.



Einthoven and Geluk proved that the first sound over the apex begins with the period of tension in the ventricle, whereas the first sound over the aorta and pulmonary artery begins with the opening of the semilunar valves. According to them the beginning of the first sound over the arterial valves could be used to mark the moment when these valves open. It seems very probable to us that the initial vibrations are caused by transverse vibrations in the walls of the ventricles during the period of tension in the muscle fibres, and the main vibrations are caused by the addition to these vibrations of vibrations set up in the atrio-ventricular valves and in the walls of the aorta and pulmonic artery at the moment at which the semilunar valves open and the sudden increase in pressure in these vessels results.

It must be admitted that there is no conclusive evidence for this idea and we wish to point out that if the observation of Hering<sup>10</sup> is confirmed, that the papillary muscles contract 0.01-0.03 sec. before the ventricular walls, then perhaps the initial vibrations could be explained as the result of transverse vibrations of the atrio-ventricular valves caused by the contraction of the papillary muscles. Only in the case of de W. on the one day is there some justification for the assumption that the initial vibrations, or "Vorton," are due to auricular contraction. In the case of de W. the initial vibrations begin at the apex 0.03-0.04 sec. before the ventricular electrocardiogram. But the interval between the beginning of the initial and the beginning of the main vibrations is still shorter here than in those pathological cases where there is an audible auricular sound, as for instance in mitral stenosis. We refer the reader to Fig. 8 of Einthoven's paper upon the recording of the heart sounds with the string galvanometer.<sup>2</sup> This phonocardiogram, taken over the apex of a patient with mitral stenosis, shows a presystolic murmur coming about 0.2 sec. before the first sound.

For the sake of clearness and simplicity in the presentation of our results we have constructed four tables. Table 1 presents the results of measurements made upon the phono-electrocardiogram; the phonocardiogram, and the electrocardiogram by lead *I*. The sounds were recorded over the apex. The initials of the persons investigated and the numbers of the plates used for the measurements are contained in the first vertical column. In the second vertical column we find the time interval from the beginning of the ventricular electrocardiogram to the commencement of the first sound. The initial vibrations are taken as the commencement of the first sound in all cases where they are to be made out with certainty. The time interval from the summit of *R* to the commencement of the first sound stands in the third vertical column. A minus sign before this value means that the first sound begins before the summit of *R* is reached. In the fourth column we find the time interval from the end of *T* to the commencement of the second heart sound. Table 2 contains the same results as table 1, except that the results were obtained with lead *II*. Table 3 corresponds to tables 1 and 2, the lead being here *III*. The numbers in any horizontal row were obtained from negatives taken one after the other as fast as possible.

The values in corresponding horizontal rows of the three tables were obtained from measurements made on negatives taken from the same person, on the same day, the four plates used in getting the values for table 3 being taken as fast as possible after the four plates used for calculating the corresponding column of table 2, and these four plates having been taken as fast as possible after the four plates used for table 1.

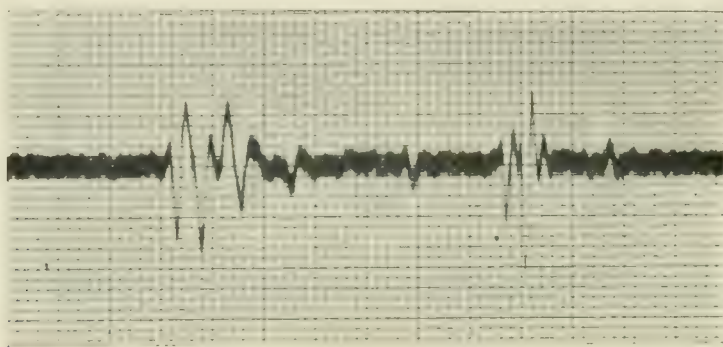


Fig. 8. Aortic sounds of de W.. July the 8th. Here the string is not free from accidental vibrations during diastole so that it is not possible to make out the initial vibrations with surety, though they seem to be here also.

The fourth table presents the results of the investigation of the time of commencement of the first sound over the apex, in the second intercostal space to the right, and in the second intercostal space to the left of the sternum. In this table the first vertical column gives the initial of the person and the numbers of the plates used. The second vertical column contains the time interval from the summit of *R* to the commencement of the first sound over the apex, the third vertical column contains the time interval from the summit of *R* to the first sound in the second intercostal space to the right, and the fourth column contains the interval from the summit of *R* to the commencement of the first sound in the second intercostal space to the left of the sternum. The fifth vertical column contains the time from the commencement of the first sound over the apex to the commencement of the first sound over the aortic valve, and the sixth column shows how much later the first sound begins in the second left intercostal space than over the apex. The negatives from which the calculations for any horizontal column of this table were made were also taken as fast as possible one after the other.

If we direct our attention to the second vertical column of the three first tables we see that there are individual differences of as much as 0.03 sec. for the interval from the beginning of the electrocardiogram by a given lead and the commencement of the first heart sound at the apex. Thus a sound of sufficient intensity to be recorded is present over the apex of de W. only 0.01 sec. after the beginning of the ventricular electrocardiogram by lead *I*; whereas with Br. the first sound over the apex is not recorded until 0.04 sec. after the beginning of the action current in the ventricle by this same lead.



TABLE I.  
TIME RELATIONS BETWEEN ELECTROCARDIOGRAM AND FIRST APEX  
SOUND BY LEAD I.

| Initials of person and<br>numbers of plates<br>used. | Time interval from<br>beginning of electro-<br>cardiogram to<br>beginning of first sound. | Summit of <i>R</i> to<br>beginning of first<br>sound. | End of Peak <i>T</i> to<br>beginning of second<br>sound. |
|--|---|---|--|
| Bl. V. 446,<br>V. 450, V. 449                        | 0.020 ± 0.001   | —0.0055 ± 0.001                                       | 0.0275 ± 0.0025  |
| Br. V. 477,<br>V. 478, V. 479                        | 0.040 ± 0.001   | 0.008 ± 0.001   | 0.02 ± 0.003   |
| Fa. V. 463<br>V. 465, V. 466                         | 0.030 ± 0.002   | 0.014 ± 0.002   | 0.02 ± 0.005   |
| On. V. 528,<br>V. 529, V. 530                        | 0.028 ± 0.002   | —0.002 ± 0.002  | 0.027 ± 0.005  |
| de W. V. 454,<br>V. 458, V. 459.                     | 0.0085 ± 0.003  | —0.0115 ± 0.003                                       | 0.020 ± 0.003  |

TABLE II.  
TIME RELATIONS BETWEEN ELECTROCARDIOGRAM AND FIRST APEX  
SOUND BY LEAD II.

| Initials of person and<br>numbers of plates<br>used. | Time interval from<br>beginning of electro-<br>cardiogram to<br>beginning of first sound. | Summit of <i>R</i> to<br>beginning of first<br>sound. | End of <i>T</i> to<br>beginning of second<br>sound. |
|--|---|---|---|
| Bl. V. 444,<br>V. 445, V. 446,<br>V. 448             | 0.038 ± 0.001   | —0.0105 ± 0.001                                       | 0.034 ± 0.005                                       |
| Br. V. 480,<br>V. 482, V. 483                        | 0.028 ± 0.002   | —0.012 ± 0.002  | 0.011 ± 0.005                                       |
| Fa. V. 463, V. 464,<br>V. 469, V. 470                | 0.040 ± 0.002   | 0.003 ± 0.002   | 0.008 ± 0.005                                       |
| On. V. 523,<br>V. 524, V. 441                        | 0.028 ± 0.001   | —0.011 ± 0.001  | 0.03 ± 0.005  |
| de W. V. 453,<br>V. 454, V. 455,<br>V. 456           | 0.020 ± 0.003   | —0.015 ± 0.003  | 0.001 ± 0.003                                       |

TABLE III.

TIME RELATIONS BETWEEN ELECTROCARDIOGRAM AND FIRST APEX  
SOUND BY LEAD *III*.

| Initials of person and<br>numbers of plates<br>used. | Time interval from<br>beginning of electro-<br>cardiogram to<br>beginning of first sound. | Summit of <i>R</i> to<br>beginning of first<br>sound. | End of Peak <i>T</i> to<br>beginning of second<br>sound. |
|--|---|---|--|
| Bl. V. 446,<br>V. 451, V. 452                        | $0.040 \pm 0.001$   | $-0.0105 \pm 0.005$                                   | $0.046 \pm 0.005$  |
| Br. V. 484,<br>V. 485, V. 481                        | $0.043 \pm 0.001$   | $-0.001 \pm 0.001$                                    | $0.005 \pm 0.02$   |
| Fa. V. 467,<br>V. 468, V. 463                        | $0.042 \pm 0.002$   | $0.004 \pm 0.002$                                     | $0.004 \pm 0.005$  |
| Ou. V. 526,<br>V. 527, V. 525                        | $0.026 \pm 0.001$   | $-0.010 \pm 0.001$                                    | $0.024 \pm 0.005$  |
| de W. V. 460,<br>V. 461, V. 462,<br>V. 454           | $0.017 \pm 0.003$   | $-0.012 \pm 0.003$                                    | $0.008 \pm 0.005$  |

If, on the other hand, we wish to get an idea of the length of the interval between the beginning of the action current in the ventricle and the first heart sound, we must take the largest value in any one of the three leads, because the beginning of the electrocardiogram does not fall in exactly the same phase of the heart beat by each lead. Thus we see the first heart sound of Bl. beginning 0.02 sec. after the beginning of the action current by lead *I*, and 0.04 sec. after the action current by lead *II*. This means that the first heart sound of Bl. appears 0.04 sec. after the earliest record of the beginning of the action current of the ventricle which we are able to get. The first heart sounds of Bl., Br., and Fa. come 0.04 sec. after the first indication of the action current of the ventricle; the first sound of Ou. comes 0.03 sec., and the first heart sound of de W. comes 0.02 sec. after the first indication of the action current of the ventricle. We are not in a position to say with certainty why there is this large difference between the values for the first three individuals and this value for de W. Certainly one of the causes is the lack of intensity of the initial vibrations in the first heart sounds of the three first individuals. For example, de W. has clear initial vibrations in the first apex sound of the records used for the determination of the time interval for his case. These initial vibrations come 0.02 sec. before the main vibrations. On the other hand out of nine first apex sounds of Br. only four show initial vibrations, coming about 0.02 sec. before the final vibrations. We did not make use of the initial vibrations in determining the values for Br. because they were very small and were not present in all the first apex sounds. If we had made use only of those sounds which showed the initial vibrations, then the first heart sound of Br. appears also 0.02 sec. after the beginning of the action current in the ventricle. Fa. also shows no initial vibrations in the records taken for tables 1, 2 and 3, but on another day, when the records



for table 4 were taken, he shows very clear and definite initial vibrations, as may be seen by looking at Fig. 9. On this day the first heart sound over the apex begins 0.02 sec. after the first indication of an action current of the ventricle by lead *II*. In many of our phonocardiograms it is very possible that we should have discovered initial vibrations if there had been no vibration of the string during diastole. These accidental vibrations though slight in themselves are enough to make the discovery of initial vibrations uncertain. Before leaving this subject we wish to refer to the one published record of Bull<sup>1</sup> where the first heart sound comes about 0.03 sec. after the beginning of the ventricular electrocardiogram.\* We believe that we are justified in saying that the first heart sound appears over the apex 0.02-0.03 sec. after the first indication of the action current of the ventricle.

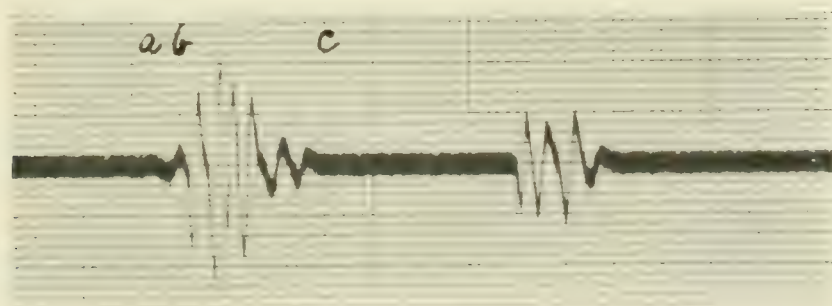


Fig. 9. Apex phonocardiogram of Fa. Stethoscope in fifth intercostal space in mamillary line. Fa's apex beat lies 1 cm. outside mamillary line. *ab* are the initial vibrations.

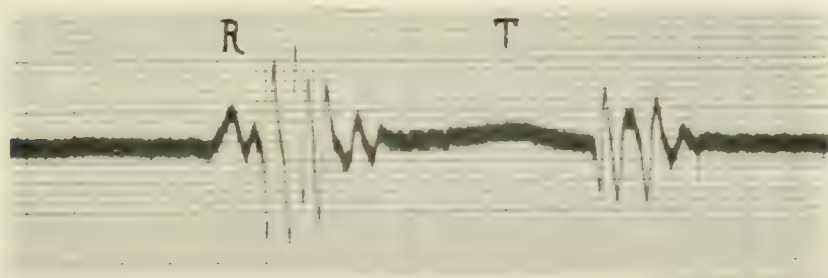


Fig. 10. Phono-electrocardiogram corresponding to Fig. 9. Lead *II*.

Our measurements show that the electrocardiogram by different leads begins in different phases of the heart beat. Einthoven<sup>2</sup> has shown that the time interval between the peaks differs in the different leads and that peaks with the same name, but taken by different leads, fall in slightly different phases of the heart beat. He has shown that though the formula lead *II* – lead *I* = lead *III* is theoretically correct, yet there is some difficulty in seeing this directly in the recorded electrocardiograms; if we subtract the height of say peak *RI* from that of peak *RII* we do not always obtain the height of peak *RIII* exactly, because these three peaks do not all come in precisely

\*Bull gives 0.04 sec. for the interval, whereas 0.03 seems better to us.

the same phase of the cardiac cycle. We are now in a position to test the formula with greater accuracy, for we can take a given point of the heart sound as a fixed point in the cardiac cycle and can subtract synchronous ordinates of the electrocardiogram of lead *I* from the corresponding ordinates of lead *II*, and can compare these values with the values found for the synchronous ordinates of lead *III*. We have done this for the electrocardiograms of four persons and find good agreement between the values for the synchronous ordinates of lead *III* as calculated from leads *I* and *II* and the values of the ordinates as measured directly in the record of lead *III*.

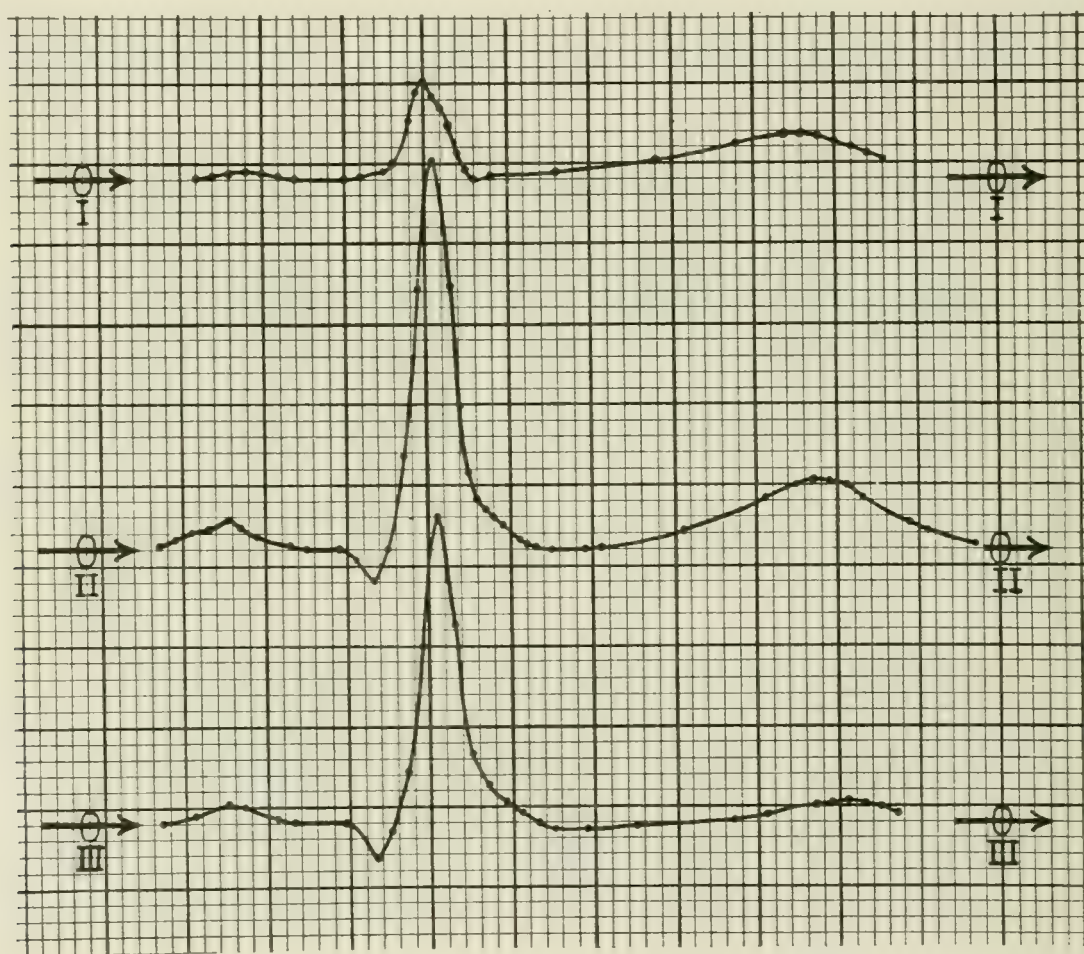


Fig. 11. Electrocardiogram of Bl. by leads *I*, *II* and *III*. These electrocardiograms were constructed by measuring the heights of the ordinates of the original electrocardiograms and constructing therefrom the corresponding ordinates of Fig. 2. Corresponding ordinates of the constructed electrocardiograms represent the same phase of the heart's cycle. Ordin. 1 sec. div. =  $1 \times 10^{-4}$  volts. Absc. 1 sec. div. = 0.01 sec.

In Fig. 11 and 12 we reproduce the electrocardiograms of two persons which were constructed from the original records of these persons. The records from which these curves were constructed were made with especial care, so that the values of the ordinates of the records are 1 mm. equal to  $1 \times 10^{-4}$  volts, with no greater error than 2 per cent. In constructing the curves of Fig. 11 and 12 it was necessary to select electrocardiograms that were taken in exactly the same phase of respiration, as the heights of the



peaks undergo conspicuous changes during inspiration and expiration and the changes in lead *I* are opposite in direction to those in lead *III*.<sup>4</sup> We measured the ordinates corresponding to thirty or more points of the abscissæ in each of the three records and then constructed points upon squared paper corresponding to the values of the measured ordinates and the corresponding abscissæ for each lead, in such a way that points of the three leads lying on the same vertical line of the squared paper represent the height of the electrocardiogram of each of these leads for the same phase of a cardiac cycle. A curve was drawn through each system of points. In drawing these curves

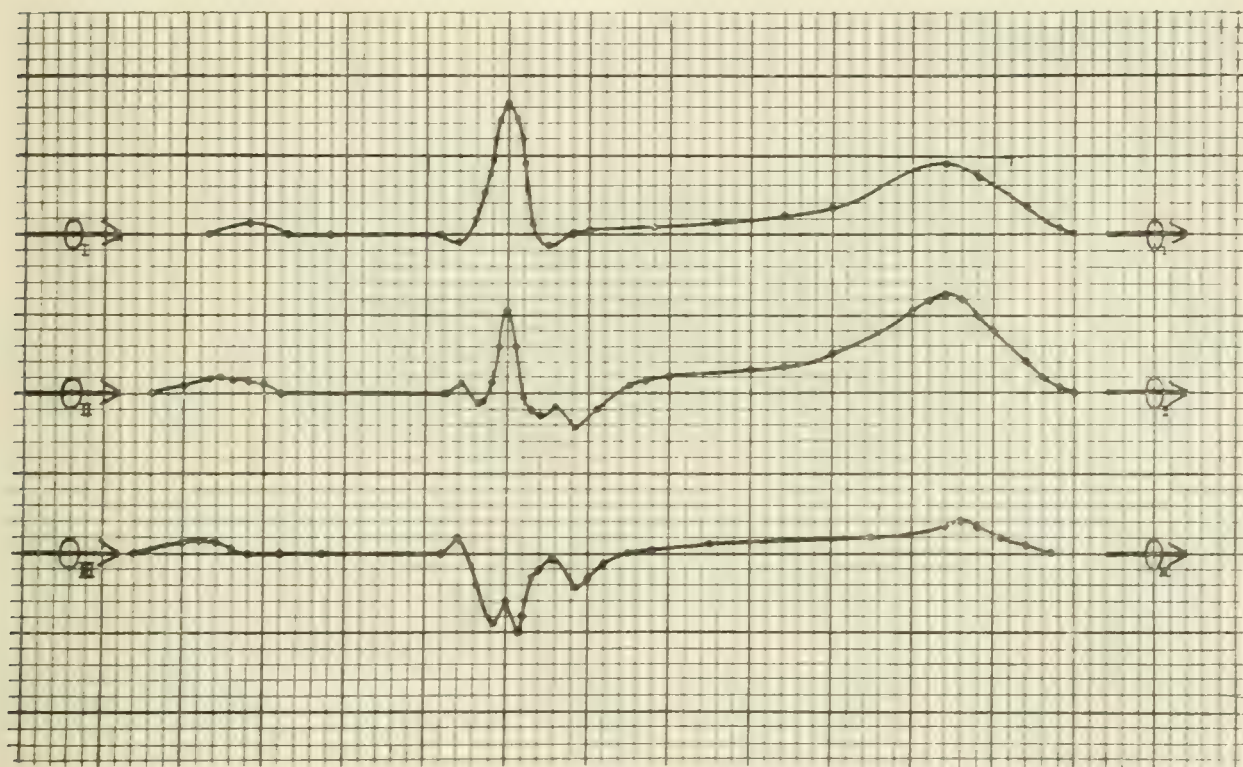


Fig. 12. Constructed electrocardiograms of Th.. Construction same as for Fig. 11. Th. is a renowned Dutch athlete with a little hypertrophy of the left ventricle.

we constantly referred to the original records in order to represent the real slope of the electrocardiogram record as exactly as possible. One scale division of the abscissæ of the curves corresponds to 0.01 sec., and one scale division of the ordinates corresponds to  $1 \times 10^{-4}$  volts, as in the original records. The arrows indicate the line of zero potential or the line of diastole. The constructed curves are reproduced nearly twice as large as the original records, in order to show more plainly the exact confirmation of the rule  $\text{lead II} - \text{lead I} = \text{lead III}$ . If we remember that an error of 0.4 mm. is possible in the height of a peak *R* of 20 mm., and furthermore that slight changes in the position of the zero line may take place during the recording of an electrocardiogram, the agreement between the values of any ordinate of the curve of lead *III* with the value calculated from the corresponding

ordinates of lead *II* and lead *I* is remarkably good. An error of 0.003 sec. in the determination of the time relations of peak *R* in the three different leads would lead to differences of 2-3 mm. in the values of the ordinates of the steeper portions of *Q* and *R* in Fig. 11 and to differences of 1-2 mm. in the heights of the ordinates of the steeper portions of the *QRS* group of Fig. 12. As the agreement between the value of the ordinates of the steeper parts of the *QRS* group, as calculated for lead *III* from the constructed leads *II* and *I*, and the height of the corresponding ordinate of the constructed lead *III* is very much better than 2-3 mm. in the case of Fig. 11, and very much better than 1-2 mm. in the case of Fig. 12, we can conclude that in these cases at least our time measurements were more exact than 0.003 sec..

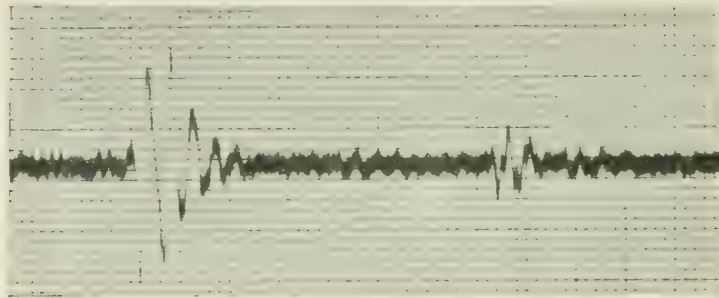


Fig. 13. Aortic phonocardiogram of Fa.. The initial vibrations seem present here also, but it is not possible to determine this with certainty because of the accidental vibrations of the string in the period between first and second sounds.

In the third vertical column of tables 1, 2, and 3 we find the time relation of the first sound over the apex to the summit of *R*. Kahn<sup>13 & 14</sup> found that the first sound begins at the end of *R* or not more than 0.01 sec. before it. The fact that he found the first heart sound beginning in the descending branch of *R* or even at the end of *R*, led Kahn to accept the hypothesis of Nicolai,<sup>17 & 18</sup> according to which the peak *R* is an expression of the activity of the papillary muscle system. Kahn only used lead *II*, in recording the phono-electrocardiogram, and therefore only the results in the third column of table 2 may be compared with those of Kahn. Excepting the case of Fa., the first sound comes before the top of *R* in all the phono-electrocardiograms used in the construction of table 2; this is seen even in the phono-electrocardiogram of Br., where the initial vibrations were not used because they were not always present, and when present were very small, the first sound comes 0.01 sec. before the summit of *R*. For the one exception, Fa., it may be again stated that on another day when the initial vibrations were present, and were well defined, the first heart sound over the apex begins 0.017 sec. before the summit of *RII*.

The reason why Kahn found the first sound coming after the summit of *R* is to be sought in the fact that Kahn's string was never free from accidental



vibrations during the interval following the second heart sound, and it was therefore impossible to distinguish the small beginning vibrations of the first heart sound from the accidental vibrations due to noises in the room or to other causes. Our results as well as the one published curve of Bull seem to speak against the views of Nicolai. We must assume that a short time elapses between the action current of the heart muscle and the beginning of a sound produced by the contraction of that muscle, for some time must elapse before the contraction of the muscle has advanced far enough to produce an audible or recordable sound. We find the first sound at the apex coming in almost all cases 0.01 sec. before the summit of *R* in at least one of the leads, and believe that *R* is the expression of the action current corresponding to the muscle contraction which produces the first sound. It seems hardly probable that either the muscle sound of the papillary muscle itself, or the sound caused by the tension on the atrio-ventricular valves due to the contraction of the papillary muscle, could have sufficient intensity to be recorded by our apparatus.

In the last vertical column of the first three tables we see that the second sound begins 0.010-0.02 sec. after the end of *T* in general, though in some cases the sound comes even closer after the end of *T*. As these measurements are not more accurate than 0.005-0.01 sec. we do not wish to draw any conclusions from them. It is not at all strange though that the second sound comes just at the end of *T* or even before it. *T* represents the relaxation of a large part of the musculature of the ventricle and the period of falling pressure in the ventricle. It ends therefore at about the time when the semilunar valves close and the second sound begins. The semilunar valves will close before all the musculature is relaxed and the second sound might well come before the end of *T*. Bull's single published curve shows the second sound beginning less than 0.01 sec. after the end of *T*.

We shall now consider the results contained in the fourth table. In all five cases the first sound begins earlier over the apex than over the second intercostal spaces. The apex phonocardiograms of Bl., Fa., and Ou. show initial vibrations without any doubt and in these cases the first sound over the apex begins 0.02-0.04 sec. before the first sound over the second intercostal spaces to right and left. These sounds over the semilunar valves begin at practically the same time, the small differences found being within the error of the measurement. Kahn found similar differences between the time of commencement of the first sound over the apex and commencement of the first sound over the second intercostal spaces. Einthoven in the case previously mentioned found a difference of 0.06 sec.. In the case of de W. we find a still larger difference, namely 0.1 sec.. The first sound of de W. over the second intercostal spaces shows a small but clearly defined peak coming 0.06 sec. before the rest of the sound. This peak represents without any doubt the deep peak of the initial vibrations of the first apex sound.\*

---

\* See Figs. 4, 6, 8.

TABLE IV.

TIME INTERVAL SUMMIT OF *R* TO BEGIN FIRST SOUND OVER APEX, OVER AORTIC VALVE AND OVER PULMONARY VALVE. LEAD II.

| Initial of person and numbers of plates used.   | Summit <i>R</i> to beginning of first sound at apex. | Summit <i>R</i> to beginning of first sound over aorta. | Summit <i>R</i> to beginning of first sound over pulmonary artery. | First apex sound earlier than first sound over aortic valves. | First apex sound earlier than first sound over pulmonary artery. |
|---|--|---|--|---|--|
| Bl. V. 531,<br>V. 532, V. 533,<br>V. 534, V. 535,<br>V. 536, V. 537,<br>V. 538                      | $-0.0029 \pm 0.001$                                  | $0.0233 \pm 0.001$                                      | $0.0259 \pm 0.001$   | 0.0262  | 0.0280   |
| Br. V. 486,<br>V. 487, V. 489,<br>V. 490, V. 491,<br>V. 492, V. 493                                 | $0.0060 \pm 0.002$                                   | $0.014 \pm 0.002$                                       | $0.015 \pm 0.002$  | 0.008   | 0.009  |
| Fa. V. 503,<br>V. 504, V. 505,<br>V. 506, V. 507,<br>V. 508, V. 509,<br>V. 510                      | $-0.0172 \pm 0.002$                                  | $0.0192 \pm 0.005$                                      | $0.0217 \pm 0.005$   | 0.0364  | 0.0389   |
| Ou. V. 512,<br>V. 513, V. 515,<br>V. 516, V. 517,<br>V. 518, V. 519,<br>V. 520                      | $-0.0035 \pm 0.002$                                  | $0.027 \pm 0.002$                                       | $0.0228 \pm 0.003$   | 0.0305  | 0.0263   |
| de W. V. 555,<br>V. 556, V. 557,<br>V. 558, V. 559,<br>V. 560, V. 561,<br>V. 562, V. 563,<br>V. 564 | $-0.0745 \pm 0.001$                                  | $0.021 \pm 0.001$                                       | $0.0281 \pm 0.001$   | 0.0955  | 0.1026   |

Between this small peak and the rest of the first sound over the semilunar valves, there is a period in which the string is quiet because the sound over the semilunar valves, corresponding to the initial vibrations at the apex, is too weak to be recorded when the sounds over the semilunar valves are recorded. If we had used more current, perhaps we should have seen these initial vibrations in the larger first sounds to be obtained thereby over the semilunar valves, but we are not sure of this because in the first place it is impossible under the circumstances to get a quiet string in the period following the second sound, and the small initial vibrations would be masked by the accidental vibrations; and in the second place because it is possible that the microphone membrane would not react to so slight a sound. The one peak of the initial vibration, as seen in the first sound of de W. over the second intercostal spaces, has exactly the same form as the corresponding vibration of the first sound over the apex; and we believe that, if the method would allow of the recording of weaker sounds, then the initial vibrations would be present in all first heart sounds recorded over the second intercostal spaces, and that there would not be a large difference in the time of its commencement



over the apex and over the semilunar valves. We have many examples of initial vibrations which are clearly present in the first heart sound recorded over the apex and which may be found in the first heart sound recorded over the second intercostal spaces by careful inspection and comparison of the two sets of curves. We believe that we are justified in saying that the first sound over the apex, as usually recorded, begins 0.02-0.04 sec. before the first sounds over the semilunar valves, but this is due to the fact that the first sound begins with one or two vibrations of small amplitude and slow period,

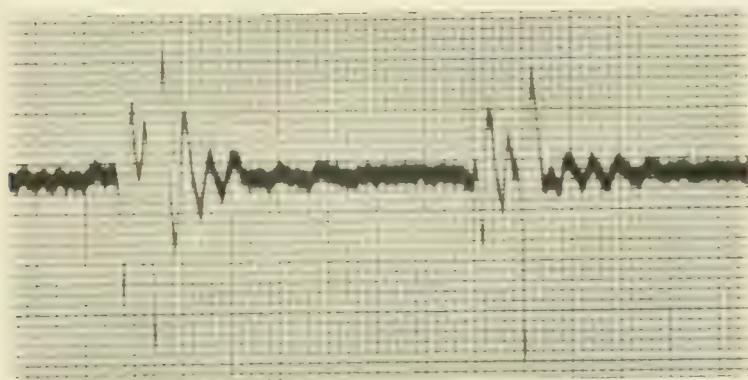


Fig. 14. Pulmonic phonocardiogram of Fa.. Here no initial vibrations can be made out because of the unquietness of the string.

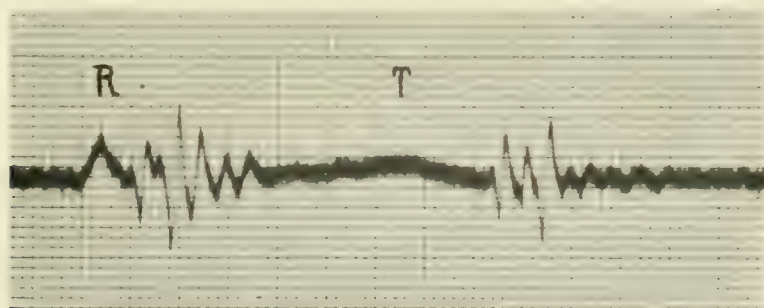


Fig. 15. Phono-electrocardiogram corresponding to Fig. 12. Lead II.

which are only intense enough over the apex to be recorded there ; whereas they are so weak over the second intercostal spaces that they are not present in the records taken from over these spaces, or if really present in these records are not to be distinguished from the vibrations due to accidental noises in the room or to vibrations as a result of the strong current passed through the microphone. By careful study of the curves of the first heart sound over the semilunar valves, where no accidental vibrations are present or where when present they are so small that there is no difficulty in making out the initial vibrations, we can almost always find them. It is very difficult to get curves of the heart sounds over the

second intercostal spaces which are free from accidental vibrations, for we must use stronger currents in order to record the sounds over these spaces. According to our idea it is only the weakening of the initial vibrations of the first heart sound in conduction to the second intercostal spaces which gives rise to a difference in the time of appearance of the first sound over the apex and over the second intercostal spaces. It is not to be wondered at that Weiss did not find a difference in the time of commencement for the first heart sound over the apex and for the first heart sound over the second intercostal spaces because the oscillations recorded by him have so small an amplitude that the small initial vibrations could not be seen. On the other hand Bull's records show the initial vibrations very clearly.

### RESUMÉ.

1. The first heart sound begins with one or more vibrations of longer period and much smaller amplitude. These initial vibrations are followed by a number of vibrations of shorter period and larger amplitude. The initial vibrations run continuously into these larger vibrations. The initial vibrations are not to be seen in most of the records of heart sounds taken from the second intercostal spaces.

2. The first sound at the apex begins 0.02-0.04 sec. before the commencement of the first sound over the second intercostal spaces. This is because the initial vibrations are poorly transmitted to the region over the great vessels and therefore cannot be easily recorded there.

3. The initial vibrations correspond closely to the period of rising tension in the ventricle and the following vibrations correspond to the beginning of the emptying of the ventricle ; consequently we have a means of telling very closely when the heart begins to contract and when the pressure in the ventricles is equal to that in the large arteries and the emptying begins.

4. The first sound over the apex begins 0.01 sec. before the summit of *R* is reached, when the initial vibrations are recorded, otherwise after the summit of *R* and in its catacrotic limb. The *QRS* group is the expression of the contraction of the heart wall.

5. The first sound begins about 0.02-0.03 sec. after the first indication of the action current of the ventricle.

6. The summits of *R* in the three leads fall in slightly different phases of the heart beat.



7. The rule that lead *II* – lead *I* = lead *III* is proved experimentally.

8. The heart sounds have not an absolutely constant form from one beat to another. The sound form, though remaining practically the same to superficial examination, changes somewhat, so that the time interval between two easily recognisable peaks of the recorded sound varies one or two thousandths of a second from beat to beat. The relative intensity of the peaks changes from beat to beat also.

The theme of this paper was suggested to us by Professor Einthoven and our thanks are due to him for his unfailing kindness and help throughout the work. We are also very much indebted to Mr. A. de Waart, assistant in the laboratory, for his aid in carrying out the experimental part of this work.

#### BIBLIOGRAPHY.

- <sup>1</sup> BULL. Quart. Journ. exper. Physiol., 1911, iv, 289.
- <sup>2</sup> EINTHOVEN. Archiv. f. d. ges. Physiol., 1907, cxvii, 461.
- <sup>3</sup> EINTHOVEN. Archiv. f. d. ges. Physiol., 1909, cxxx, 287.
- <sup>4</sup> EINTHOVEN. Lancet, 1912, i, 853.
- <sup>5</sup> EINTHOVEN AND GELUK. Archiv. f. d. ges. Physiol., 1894, lvii, 617.
- <sup>6</sup> FRANK. München. med. Wochenschr., 1904, li, 953.
- <sup>7</sup> FRANK. Zeitschr. f. Biol., 1905, xlvi, 524 and 441.
- <sup>8</sup> GERHARTZ. Archiv. f. d. ges. Physiol., 1910, cxxxi, 509.
- <sup>9</sup> GERHARTZ. "Die Registrierung des Herzschalles," Berlin, 1911.
- <sup>10</sup> HERING. Archiv. f. d. ges. Physiol., 1909, cxxvi, 225.
- <sup>11</sup> HÜRTHLE. Zentralbl. f. Physiol., 1904, xviii, 617.
- <sup>12</sup> HÜRTHLE. Archiv. f. d. ges. Physiol., 1895, lx, 263.
- <sup>13</sup> KAHN. Archiv. f. d. ges. Physiol., 1909, cxxix, 291 and 597.
- <sup>14</sup> KAHN. Archiv. f. d. ges. Physiol., 1910, cxxxiii, 597.
- <sup>15</sup> LOW. Philosoph. Magazine, 1894, xxxii, 249.
- <sup>16</sup> MAREY AND CHAUVEAU. Mém. d. l'Acad. d. Med., 1861, xxviii.

- 17 NICOLAI. Zentralbl. f. Physiol., 1907, XXI, 678.
- 18 NICOLAI. Nagel's Handbuch, d. Physiol. d. Menschen, 1909, I, 824.
- 19 TIGERSTEDT. Ergebnisse d. Physiol., 1909, VIII, 592.
- 20 WEISS. Archiv. f. d. ges. Physiol., 1908, CXXIII, 341
- 21 WEISS. "Phonokardiogramme," Jena, 1909.



OBSERVATIONS UPON A CURIOUS AND NOT UNCOMMON FORM  
OF EXTREME ACCELERATION OF THE AURICLE.  
"AURICULAR FLUTTER."

BY THOMAS LEWIS.\*

(*Cardiographic Department, University College Hospital  
Medical School*).

*Introductory Remarks.*

FOUR years ago Hertz and Goodhart<sup>1</sup> published the notes of a case in which it was evident that the auricles had assumed a very rapid action. The case was one in which the auricles contracted at a rate varying between 216 and 234 per minute, while the ventricular action was slow. Isolated cases of a similar nature have since been recorded by Jolly and Ritchie,<sup>2</sup> by Rihl,<sup>9</sup> and by myself.<sup>7</sup> The condition has been regarded by those interested in the recent progress of cardiac investigation as a rare affection.

While patients in whom a slow or irregular ventricular action have been more and more extensively investigated by means of graphic methods, the necessity for a routine examination of simple cardiac accelerations in the same manner has not been recognised.

It appears, as I hope to show in the present communication, that extreme acceleration of the auricular contractions to a rate of 300 per minute is not an infrequent human malady; and that the combined picture of auricular acceleration and heart-block is relatively common. It will also become apparent that if the routine examination of patients who present rapid heart action by modern methods, and especially by electrocardiographic means, is not undertaken, the condition will often escape detection.

A series of cases which has recently come under the observation of the writer has clearly shown, not only that such examination is imperative if the true nature of a given tachycardia is to be ascertained, for such cases may readily pass for other and more simple forms of acceleration, but that a detailed acquaintanceship with the forms which the electrocardiographic curve may take is essential. In most instances there are few or no signs of the extreme auricular acceleration, other than those found in the electrocardiographic pictures; and in many of these, the degree of acceleration is by no means obvious if such curves are hastily scanned. The reason for the obscurity of the signs is twofold, for, in the first instance, the auricular contraction rate is usually double the ventricular, and alternate auricular systoles are buried in the ventricular systole and pass unnoticed; and, in the second instance, the systoles of the auricles have little mechanical effect upon the blood content of either veins or ventricles, and the movements of the auricular walls are small.

---

\* Working under the tenure of a Beit Memorial Fellowship.

That acceleration of a regularly contracting auricle to a rate of 300 and even 330 per minute has frequently remained unsuspected in the past, may seem remarkable, but nothing is more certain than that such is the case and that the auricles may pursue this hurried movement so covertly that none of the older methods of examination can discover it.

It is my purpose in the present communication to show that the condition is relatively common; to point out the signs, be they arterial, venous or electric by which the malady, as it commonly presents itself to our notice, may be recognised; and further, to describe it as an affection which must stand, for clinical if not for pathological purposes, in a category of its own. The need for isolating it in this manner from other disturbances of heart mechanism is impressed by its special relations to certain forms of abnormal heart action, by the peculiar course which it pursues and by the curious manner in which it reacts to remedies.

For the reasons stated, it seems expedient that the disorder should be regarded as a distinct type, and that it should be treated separately even though complete separation may not be possible from new rhythms which, though of auricular origin, are of lower grade. The readiest means of isolating it in this manner is to apply to it a distinctive name, and there seems none better than that adopted by Jolly and Ritchie in the description of their case, namely, "auricular flutter"; for this term aptly describes the essential condition, it avoids reference to the varying grades of ventricular response and clearly serves to distinguish it from the allied disorder, "auricular fibrillation." The distinction from tachycardia of lower rate, though also of auricular origin, is more arbitrary, though I think essential at the present time. The auricular rate may be increased to any figure intermediate between 72 and 335 beats per minute; but there are certain features which accelerations of over 200 appear to hold in common; and so, even if the distinction subsequently proves not to be strictly valid on the pathological side, the separation is not without merit from the clinical standpoint.

In the following pages, I propose to deal in the first place with my own observations; secondly to summarise former observations and to revise certain previous reports; and, finally, to discuss in a general account the disorder as a clinical entity.

### *Observations.*

**CASE 1.** M., a married woman, aged 50, came under observation on April the 19th, 1912.

*Past history.* There had been six children; one child died at three months of age of "rheumatic fever." The patient was affected by rheumatic fever herself when this child was born; she was then 23 years of age.

*History of cardiac condition.* She had suffered from shortness of breath for eleven years. For four months it had been more severe, being especially noticeable after exertion. Palpitation had been present for four months, and there was also some pain in the precordial region. Her feet had never swollen; there had never been hæmoptysis. Two months before admission, while lifting a heavy saucepan, she had a feeling "as if her heart was displaced": she experienced great breathlessness and palpitation at the time and took to bed. It was the first attack of its kind.



*Condition.* April the 19th, 1912. A stout woman, who showed a trace of cyanosis. Breathlessness was obvious while she lay flat in bed. There was no dropsy. The liver dulness came an inch below the costal margin; the organ was readily felt, and there was tenderness to pressure over it. The urine was normal. During her stay she had fever for a few days (97-101 degrees Fahr.) and the ankle and wrist joints became swollen and painful.

The limits of cardiac dulness lay 2 and 5 inches to the right and left of the mid-sternal line. A short systolic murmur was heard at the apex. The heart sounds were otherwise normal. At the time of observation, she was upon thirty minims of the tincture of digitalis and she had had in all seven and a half drachms of this drug or its equivalent. The ventricular rate was usually 160, though there were periods of irregular and slower action from time to time. The rate of the heart beat was not affected by posture. The observations upon the heart mechanism and the course of the condition are summarised in the accompanying table.

| DATE                     | METHOD OF EXAMINATION.    | Vs RATE.        | As RATE. | DRUGS.                          | REMARKS.  |
|--------------------------|---------------------------|-----------------|----------|---------------------------------|---|
| 3-4-12                   | Pulse counts              | 160-118<br>-160 |          | Tinct.<br>Digit.                | Date of admission.  |
| 19-4-12                  | Electrocardiographic      | 156             | 312      | Tinct.<br>Digit.<br>m. xxx      | Chiefly 2 : 1. Also irregular periods of 2 : 1 and 3 : 1.   |
| 20-4-12<br>to<br>25-4-12 | Pulse counts.             | 120-158         |          | m. xxx<br>daily till<br>the 2nd | Usually regular; some irregular periods. Fever 101° and rheumatism of foot. Nausea.   |
| 2-5-12                   | Electrocardiographic      | 123-160         | 320      | m. xlv.                         | Chiefly 2 : 1; also irregular periods of 2 : 1 and 3 : 1.   |
| 4-5-12                   | Electrocardiographic      | 81              | 324      | m. lx                           | 4 : 1 heart-block; regular.   |
| 6-5-12                   | Electrocardiographic      | 79              |          | m. lx<br>(Total<br>dr. xviii)   | Fibrillation of the auricles.<br>Digitalis stopped.   |
| 9-5-12                   | Pulse counts              | 72-96           |          | None                            | Fibrillation still.   |
| 10-5-12                  | Pulse counts              | 88-92           |          | None                            | Fibrillation still.   |
| 12-5-12                  | Pulse counts              | 82-90           |          | None                            | Pulse became regular.<br>Probably returned to<br>normal rhythm.   |
| 13-5-12                  | Electrocardiographic      | 81              | 81       | None                            | Pulse regular, normal<br>rhythm.  |
| 15-5-12*                 | Pulse counts              | 72-92           |          | None                            | Pulse regular, normal<br>rhythm.  |
| 29-5-12                  | Electrocardiographic      | 108             | 108      | None                            | Pulse regular, normal<br>rhythm.  |
| 1-6-12                   | Electrocardiographic      | 91              | 91       | None                            | Pulse regular, normal<br>rhythm.  |
| 10-6-12                  | Pulse counts              | 70-88           |          |                                 | Normal rhythm still. The heart-<br>dullness has gone. The liver<br>has receded beneath the ribs.<br>There is no pain or puffiness.<br>She feels much stronger and<br>her colour is natural. |
| 10-6-12                  | Discharged from hospital. |                 |          |                                 |   |
| 7-8-12                   | Electrocardiographic      | 80-90           | 80-90    | None                            | Normal rhythm. Rupture healed<br>on standing and has no<br>lymphatic enlargement<br>and a little shortness of breath.   |

\* On the 15th of May, in the early morning, she had a slight stroke; consciousness was not lost but the left half of the face and left arm became paralysed and speech was impaired. The paresis cleared up entirely during the course of the next few days.

Fig. 19 is illustrative of the electrocardiograms taken during the early phases of the patient's treatment. The initial ventricular peaks are clearly defined in all leads; *T* is seen in lead *I* and slightly in lead *II*; in lead *III* it cannot be found. It is difficult to identify auricular representatives in lead *I*. In lead *II* they appear as upward deflections; the *P-R* interval seems to have a duration of about .1 sec.. In lead *III*, the shape of *P* is more complex; its general outline may be described as convex,\* the upstroke being more abrupt than the downstroke which is broken by a notch. The auricular curves are contiguous one with another, the line is never written horizontally. The auricular systoles run through the ventricular and are twice as numerous as the latter. Both chambers beat with perfect regularity, the auricles at 320 and the ventricle at 160.

Fig. 20 represents the action of the heart two days later; while under the action of digitalis heart-block had increased. In this figure the shapes of the auricular summits and their relation to each other and the ventricular systoles is more clearly seen. Both chambers still beat quite regularly but the ventricle is now contracting but a fourth as rapidly as the auricle (auricular rate 324, ventricular 81); each fourth auricular summit is buried in the opening phases of ventricular systole. The general form of both auricular and ventricular electric curves has been maintained (see Fig. 19).

Fig. 21 was taken two days later, when the auricles were fibrillating under the influence of digitalis. The ventricular action is slow (the rate was 79) but quite irregular; the regular auricular summits have given place to smaller and irregular oscillations which are most clearly seen in lead *III* (*f.f.*).

Fig. 22 shows the perfectly normal mechanism, which became established shortly after the digitalis was omitted. There is no sign of rapid and continuous oscillations in the curves; a single auricular complex occurs before each ventricular systole. The heart is beating perfectly regularly and slowly.

The series of curves is a very complete one. We have the electrocardiograms from the same heart, beating in three completely different fashions. The auricular representatives of the normal period are quite unlike those of the period of flutter. In all, the shape of the ventricular complexes is maintained in the separate leads, demonstrating quite clearly that in each instance the ventricular beats were propagated from the auricles.

*Summary.* In a woman of 50 years, an attack of rapid heart action was observed which had a probable duration of three months. The rate of the auricular contractions surpassed 300 per minute, the highest count being 324 per minute; the ventricle usually responded to alternate auricular contractions. Under high doses of digitalis the ventricular rate fell to a fourth of the auricular rate, the latter being maintained. Eventually and

---

\* The reasons for this statement are given under *CASE 3*.



TABLE OF ATTACKS IN CASE 2, COMPILED FROM A DIARY AND SHOWING THE NUMBER OF ATTACKS AND THEIR DURATION, OVER A PERIOD OF TEN YEARS.

| Year      | 1902     | 1903     | 1904     | 1905     | 1906       | 1907     | 1908     | 1909     | 1910     | 1911     | Total Number. |
|-----------|----------|----------|----------|----------|------------|----------|----------|----------|----------|----------|---------------|
| January   | 3 (17)*  | 3 (21)   | 2 (20)   | 5 (19)   | 5 (58)     | 2 (23)   | 3 (36)   | 4 (19)   | 8 (23)   | 5 (191)  | 40            |
| February  | 3 (3)    | 1 (8)    | 2 (10)   | 4 (26)   | 5 (40)     | 8 (51)   | 5 (8)    | 10 (26)  | 3 (26)   | 12 (210) | 42            |
| March     | 3 (16)   | 5 (60)   | 2 (7)    | 2 (24)   | 5 (12)     | 4 (19)   | 8 (36)   | 4 (27)   | 6 (19)   | 0        | 39            |
| April     | 3 (13)   | 2 (16)   | 2 (8)    | 4 (49)   | 6 (28)     | 7 (45)   | 3 (48)   | 4 (9)    | 5 (18)   | 1 (6)    | 37            |
| May       | 4 (5)    | 3 (9)    | 1 (13)   | 1 (14)   | 13 (63)    | 3 (39)   | 3 (14)   | 8 (31)   | 3 (3)    | 5 (51)   | 44            |
| June      | 0        | 3 (14)   | 4 (29)   | 4 (15)   | 3 (11)     | 6 (11)   | 2 (1)    | 1 (16)   | 6 (9)    | 3 (26)   | 35            |
| July      | 5 (31)   | 3 (4)    | 3 (6)    | 2 (8)    | 5 (20)     | 4 (23)   | 7 (13)   | 10 (37)  | 4 (31)   | 2 (21)   | 45            |
| August    | 1 (7)    | 4 (21)   | 2 (1)    | 12 (22)  | 9 ?        | 2 (8)    | 6 (13)   | 2 (4)    | 6 (8)    | 1 (4)    | 34            |
| September | 4 (25)   | 4 (26)   | 5 (11)   | 3 (27)   | 5 (20)     | 5 (39)   | 7 (42)   | 5 (8)    | 5 (23)   | 3 (21)   | 46            |
| October   | 2 (31)   | 4 (16)   | 2 (22)   | 5 (59)   | 6 (43)     | 3 (27)   | 2 (18)   | 8 (28)   | 3 (23)   | 10 (56)  | 45            |
| November  | 1 (10)   | 5 (38)   | 5 (47)   | 4 (34)   | 5 (62)     | 5 (55)   | 10 (66)  | 8 (22)   | 7 (46)   | 1 (16)   | 51            |
| December  | 3 (49)   | 1 (14)   | 3 (25)   | 3 (7)    | 5 (61)     | 5 (38)   | 1 (10)   | 4 (16)   | 5 (17)   |          | 30            |
| TOTALS    | 32 (207) | 38 (243) | 33 (202) | 38 (304) | 72 (401++) | 54 (378) | 57 (296) | 71 (243) | 61 (246) | 32 (634) | 488           |

\* The first figure gives the number of attacks, the second gives the total duration in hours (minutes omitted).

under the influence of the drug, the auricles fibrillated ; the digitalis was then withdrawn and in a few days the normal rhythm was restored and was maintained so long as the patient was under observation. Her symptoms were considerably relieved.

CASE 2. E. G., a clergyman, aged 65, came under continuous observation on the 2nd of February, 1912.

*Past illnesses.* He suffered from scarlet fever at 5 and 13 years of age ; on the second occasion the fever was followed by osteomyelitis of the left tibia and he was in bed for six months. At 15 he had congestion of the lungs ; and at 52 pleurisy. For three years he had been afflicted with a prostatic enlargement and had used a catheter thrice daily for three months.

*History of heart condition.* For thirty years he had been the subject of attacks of tachycardia. The first attack, at the age of 35, lasted several hours and laid him up : his doctor told him his heart was normal except for its excessive rate. Six years later, he had his second attack, and was attended for it by Dr. Bengafield, of Edmonton, who writes to me " I quite well remember him as being subject to severe attacks of tachycardia, which I could not account for. The pulse rate would go up to fully 140 or 150." From the age of 41 he had attacks each six months or each year which lasted from four to twenty hours. The attacks were accompanied by shortness of breath, a sense of precordial oppression and a feeling as if a pendulum were swinging fast in the chest. There were no anginal symptoms. The longest attacks exhausted him very much, but the shorter ones left him perfectly fit a few minutes after their cessation. He almost always continued his work if they came on while he was occupied. He often suffered from flatulence during the paroxysms. At the age of 50 he had a great deal of trouble in his parish and was much upset by it. The attacks became more frequent, commencing each week or each day. For the preceding ten years he had kept a complete diary of the attacks. From January, 1902, until November, 1912, there were 489 attacks at least. The average duration was about six hours, the shortest attack lasted a few minutes and the longest ten days. The distribution of the attacks over the ten years is seen in the table of monthly incidence on the last page. There is surprising uniformity in the distribution of the paroxysms over this period, and the totals for the several months show no seasonal incidence. A chart (page 178) of the frequency of onset during the several hours of the day and night shows the greatest frequency in the early hours of the morning, early afternoon and late evening. He attributed many of the attacks to excitement and stated that the evening attacks often followed his Sunday's sermon. He believed that meals had no relation to the attacks. The tachycardia became continuous in December, 1912, and was maintained until May, 1912.

*Condition, 6th of May, 1912.* A frail and tremulous subject. The remaining teeth were carious. There was enlargement of the prostate and infection of the bladder. The heart limits were normal, the ventricular rate was regular at 130, the sounds were normal. The arm arteries were soft : the pulse tension was not increased. Radiographic examination showed dilatation of the aorta. The auricular movements could not be seen.

The heart was examined polygraphically and electrocardiographically on a number of occasions. The general result and course may be stated in tabular fashion.

| DATE.                  | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS.                     | REMARKS.   |
|------------------------|------------------------|----------|----------|----------------------------|--|
| 29-2-12                | Electrocardiographic   | 138      | 276      |                            | 2 : 1 block.   |
| 26-3-12                | Electrocardiographic   | 96+      | 289      |                            | 3 : 1 block chiefly.<br>Ventricle a little irregular ;<br>2 : 1 periods present. |
| 2-4-12                 | Electrocardiographic   | 138      | 276      |                            | 2 : 1 block.   |
| 2-5-12                 | Electrocardiographic   | 133      | 266      |                            | 2 : 1 block.   |
| 3 <sup>rd</sup> 7-5-12 | Pulse counts           | 96-140   |          |                            |  |
| 8-5-12                 | Polygraphic            | 94       |          | Tinct.<br>Digit.<br>m. xxx | Probably 2 : 1 and 3 : 1 mixed.  |



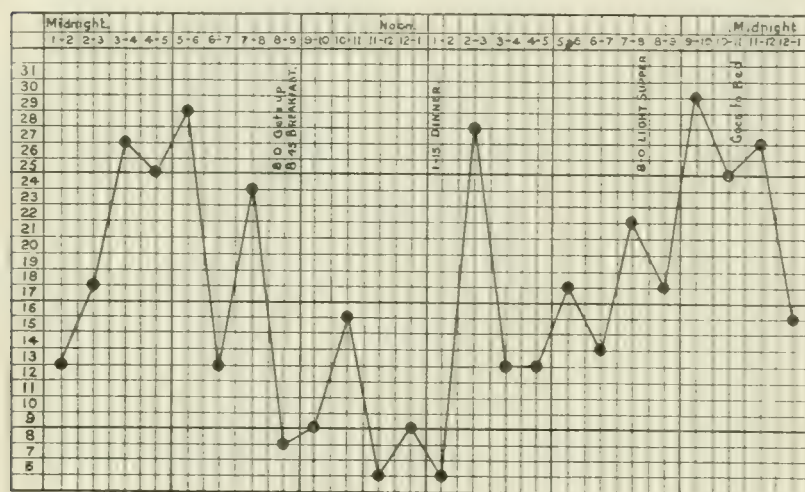
| DATE.   | METHOD OF EXAMINATION.   | Vs RATE. | As RATE. | DRUGS.   | REMARKS.   |
|---------|--|----------|----------|--|--|
| 9-5-12  | Pulse counts   | 108-112  |          | Tinet. Digit<br>m. xxx                           |  |
| 10-5-12 | Pulse counts   | 100-120  |          | m. xxx   |  |
| 11-5-12 | Polygraphic  | 92       | ? 276    | m. xxxv  | Probably 3 : 1 block   |
| 12-5-12 | Electrocardiographic   | - 137    | 274      | m. xlv   | 2 : 1 block. Occasional<br>3 : 1 and 4 : 1 periods in<br>other curves.   |
| 13-5-12 | Pulse counts   | 76-108   |          | m. l *   |  |
| 14-5-12 | Pulse counts   | 70-92    |          | m. lxxv  |  |
| 15-5-12 | Pulse counts   | 76-96    |          | m. lxxv  | } Probably 4 : 1.<br>} Pulse regular.  |
| 16-5-12 | Pulse counts   | 72-96    |          | m. c   |  |
| 17-5-12 | Electrocardiographic   | 58       |          | m. l   | Fibrillation of the auricles.  |
|         |  | 152      | ? 150    | Digit.<br>stopped.<br>(Total dr.<br>viii, m. v.) | Regular tachycardia.<br>Vomiting.  |
| 18-5-12 | Pulse counts   | 48-64    |          | None   | Auricular fibrillation.  |
| 19-5-12 | Pulse counts   | 62-68    |          | None   | Auricular fibrillation.  |
| 20-5-12 | Polygraphic  | 64       | 64       | None   | Normal rhythm. Occasion-<br>al premature beats.  |
| 21-5-12 | Electrocardiographic   | 92       | 92       | None   | Normal rhythm.   |
| 22-5-12 | Polygraphic  | 54-66    | 54-66    | None   | Normal rhythm.   |
| 23-5-12 | Passed from observation. The general condition is much improved. His breathing is fairly easy and he feels in better health. |          |          |  |  |
| 31-5-12 | Patient writes that his pulse continues to be normal.  |          |          |  |  |
| 6-6-12  | Electrocardiographic   | 102      | 102      |  | Normal rhythm. Has had<br>a few short attacks.<br>Condition of patient<br>greatly improved.  |
| 27-6-12 | Electrocardiographic   | 84       | 84       |  | The patient states he has<br>had one or two short<br>attacks of a few minutes<br>and one long one since<br>he was last seen. His<br>condition shows steady<br>improvement. |

\* Pressure upon the right or left vagus while this patient was under digitalis, produced additional slowing of the ventricle.

Fig. 23 is one of the earliest electrocardiograms taken from this patient. The auricular rate is 289 per minute. The *P* summits in lead *I* are not seen. In leads *II* and *III* they form, together, continuous wavy lines, the individual waves of which are placed regularly. It is not certain where each auricular representative starts or finishes, though it is probable, from a consideration of similar curves in other cases, that each is

convex and starts with the upstroke. The ventricular action is not quite regular and the beats have not always the same relation to the auricular representatives with which they fall; for the most the curve shows 3:1 heart-block and probably consists as a whole of 3:1 and 2:1 periods. *T* is seen to some extent in lead *I* only.

Fig. 24 was taken on the 12th of May while the patient was beginning to be influenced by digitalis. The auricular curves are similar to those of the preceding figure (rate 274), but the ventricular curves are relatively more numerous. The curve shows 2:1 heart-block for the most part; there are occasional periods of 3:1 and 4:1 block. Five days later the heart action became grossly irregular in response to fuller doses of the drug. Curves of this day are shown in Fig. 25 and 26.



A Chart showing the times of onset of 428 attacks. Compiled from a diary kept for ten years. (CASE 2, p. 176).

Fig. 25 shows a slow and completely irregular ventricular action (rate 58). The auricular waves are no longer present. *T* is clearly seen in all leads, and following the *Q*, *R* and *S* group in leads *II* and *III*, there are extra deflections from time to time, which are not understood. These curves in all probability represent auricular fibrillation, the oscillations being too small

to record. From time to time during the examination, the heart's action became rapid and perfectly regular at 152 per minute. The electrocardiograms are shown in Fig. 26. The type of the ventricular complexes is still maintained, though in leads *II* and *III* the curious deflections following the *Q*, *R* and *S* group are constantly present. No trace of auricular summits can be found; the exact meaning of this mechanism is unknown, but it probably results from simultaneous contraction in auricle and ventricle. A few days later, after the digitalis had been omitted, the normal mechanism became restored; it is illustrated by Fig. 27. Here each regular ventricular contraction is preceded by a single auricular contraction of normal type.

This series of curves is a very complete one. Four perfectly distinct mechanisms may be compared in electrocardiograms from the same patient. The auricular representatives of the normal period are unlike those of the period of flutter. The ventricular complexes maintain their general form throughout the opening phases in all; for the impulses in all are generated above the ventricle.

*Summary.* A man of 65 years had been the subject of attacks of tachycardia for 30 years (rate 140-150). Eventually the condition of rapid



heart action became established; it lasted for a period of five months; during this time the auricles were beating at a rate of approximately 280 per minute, while the ventricles responded as a rule to alternate auricular impulses. Under large doses of digitalis, and after a preliminary period in which higher grades of heart-block were seen, the auricles passed into fibrillation; the drug being withdrawn the normal rhythm was restored and was maintained so long as the patient was under observation.\* While the auricular flutter was present, the rate of contractions was uninfluenced by posture, and by digitalis administration. As a result of treatment his general condition improved very considerably.

**CASE 3.** E. B., a clergyman, aged 53, came under continuous observation on May the 14th, 1912.

*Past illnesses.* He suffered from the usual children's ailments. At the age of 41 he had diphtheria and it was followed by palatal paralysis and weakness of the limbs and eye muscles. Apart from these illnesses and his heart condition, he had always been a healthy man; hard worked and athletic, he had led a strenuous life.

*History of heart condition.* His attacks of palpitation started at the age of 16 when he was at school. The first attack came on after a hard game of football. For several years he had two or three attacks following exertion; they always started abruptly without warning and ended with equal suddenness. The attacks became more frequent when he was 20, occurring four or five times a year; excitement and exposure to cold induced them; they usually lasted twenty minutes, the longest attack was of about two hours duration. The heart action was very rapid. Following upon the diphtheria they became more frequent and more severe, exhausting him and interfering with his work. He had to change his parish, seeking lighter work.

Three years before he came under observation an attack came on after a long cycle ride, and it continued until he sought advice. During this period his pulse rate lay continuously between 140 and 160; he had been examined on numerous occasions and was under medical supervision for long periods; his chief symptoms were disinclination to exert himself and easy fatigue. These sensations and consciousness of the heart's action alone disturbed him.

*Condition on May the 14th, 1912.* A sturdy and robust man of good colour, he was a little tremulous. He showed anxiety, but this was apparently the result of his inability to follow his occupation rather than fear for his condition. The right and left limits of cardiac dulness lay 0 and 4 inches to the right and left of the mid-sternal line respectively. The heart sounds were natural, and there were no murmurs. The arteries presented no signs of thickening, the blood pressure was normal; the urine was normal. The heart's action was regular but continuously rapid.

He was seen on two occasions prior to coming under continuous observation and on both the heart's mechanism was similar. A synopsis of observations is given in the accompanying table.

| DATE.   | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS.                  | REMARKS.  |
|---------|------------------------|----------|----------|-------------------------|---|
| 10-1-12 | Electrocardiographic   | 162      | 324      | None                    | 2:1 heart-block. Auricular rate constant after exertion and after exercise.           |
| 3-5-12  | Electrocardiographic   | 156      | 312      | None                    | 2:1 heart-block. Auricular rate constant after exertion and after exercise.           |
| 14-5-12 | Polygraphic            | 135-147  | 294      | None                    | 2:1 with occasional 3:1 and 4:1 periods. (Patient has been under digitalis recently). |
| 15-5-12 | Electrocardiographic   | 156      | 312      | Nativ. Digit<br>Gran. i |   |

\* In July the patient decided upon an operation for his enlarged prostate; he was a good deal worried about it and he had a return of the flutter. The operation was performed, but he died within eight days. A post-mortem could not be obtained.

| DATE.               | METHOD OF EXAMINATION.                | Vs RATE. | As RATE. | DRUGS.                         | REMARKS.  |
|---------------------|---------------------------------------|----------|----------|--------------------------------|---|
| 16-5-12             | Electrocardiographic                  | 106      | 308      | Digit. Gran. i                 | 2 : 1, 3 : 1 and 5 : 1 irregular. Auricular rate constant after exertion and after resting.     |
| 17-5-12 and 18-5-12 | Pulse counts                          | 70-100   |          | ii                             | Very irregular.   |
|                     |                                       |          |          | ii                             | Very irregular.   |
| 19-5-12             | Polygraphic                           | 85-140   | 280      | ii                             | 2 : 1 with very frequent 3 : 1 and 4 : 1 periods (irregular). (Ventricle slower while resting). |
| 20-5-12             | Polygraphic                           | 84       | 300      | iii                            | Very irregular. 2 : 1, 3 : 1, 4 : 1 and 5 : 1 mixed. (Ventricle slow while resting).            |
| 21-5-12             | Electrocardiographic                  | 75       | 288      | iii                            | 4 : 1 and occasional 2 : 1. (Ventricle slow while resting).                                     |
| 22-5-12             | Pulse counts                          | 70-90    |          | iii                            | Very irregular.   |
| 23-5-12             | Electrocardiographic (after exercise) | 139      | 278      | iii                            | 2 : 1 after exercise. Slow and irregular while resting.   |
| 24-5-12             | Polygraphic                           | 70       | 301      | iii                            | Very irregular. 3 : 1, 4 : 1 and 5 : 1 mixed.   |
| 25-5-12             | Polygraphic                           | 114      | 296      | iv                             | 2 : 1, 3 : 1 and 4 : 1 mixed. Very irregular.   |
| 26-5-12             | Polygraphic                           | 92       | 264      | iv                             | Very irregular. 2 : 1, 3 : 1, 4 : 1 and 5 : 1 mixed.  |
| 27-5-12             | Pulse counts                          | 90-140   |          | iv                             | Pulse slow and very irregular while resting. Fast and regular while standing.                   |
| 28-5-12*            | Polygraphic                           | 74       | 280      | i Granules stopped, (total 36) | 3 : 1, 4 : 1 and 5 : 1 ; irregular.   |

\*On the 28th the patient experienced nausea and retching. There had been yellow vision and increased sensibility to auditory and touch impressions for several days. The digitalis administration had consequently to be abandoned. It was decided to try strophanthus after a few days of rest.

| DATE.   | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS. | REMARKS.  |
|---------|------------------------|----------|----------|--------|---|
| 29-5-12 | Polygraphic            | 73       | 288      | None   | 3 : 1, 4 : 1 and 5 : 1 periods mixed.                                     |
| 30-5-12 | Pulse counts           | 70-144   | 288      | None   | Pulse slow and irregular while resting ; fast and regular while standing. |



| DATE.    | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS.                                       | REMARKS.  |
|----------|------------------------|----------|----------|--|---|
| 1-6-12   | Polygraphic            | 72-144   | 288      | None   | Chiefly 4:1, but with irregular. Fast standing. No change of auricular rate with posture. |
| 3-6-12   | Pulse counts           | 80-140   |          | None   | Pulse slow and irregular while resting. Fast and regular while standing.                  |
| 4-6-12   | Pulse counts           | 70-100   | Rapid    | Tinct. Stroph. m. M                          | Pulse slow and irregular while resting. Fast and regular while standing.                  |
| 5-6-12   | Electrocardiographic   | 146      | 292      | 1 drachm                                     | Slower after lying some while.  |
| 6-6-12   | Electrocardiographic   | 142      | 284      | 1 drachm                                     | 2:1, slower and irregular on lying.   |
| 7-6-12   | Electrocardiographic   | 144      | 288      | 1 drachm                                     | 2:1, slower and irregular on lying.   |
| 8-6-12   | Electrocardiographic   | 80-142   | 284      | m. M   | 2:1 chiefly. Occasional periods of 4:1.   |
| 9-6-12   |                        |          |          | 1 drachm                                     |   |
| 10-6-12  | Electrocardiographic   | 75-142   | 284      | 1 drachm                                     | 2:1 with frequent periods of 4:1 and 5:1.   |
| 11-6-12  | Electrocardiographic   | 80-145   | 290      | 1 drachm                                     | Chiefly 2:1. Periods of 4:1 and 5:1 frequent on lying or resting.                         |
| 12-6-12  | Electrocardiographic   | 72-144   | 288      | 1 drachm                                     | Chiefly 2:1. Periods of 3:1, 4:1 and 5:1 on lying or resting.                             |
| 13-6-12  |                        |          |          | 1 drachm                                     |   |
| 14-6-12  | Electrocardiographic   | 80-139   | 278      | 1½ drachms                                   | Chiefly 2:1. Periods of 4:1 while lying or resting.                                       |
| 15-6-12  | Electrocardiographic   | 75-150   | 300      | 1½ drachms                                   | Chiefly 2:1. Periods of 3:1 and 4:1 while resting.  |
| 16-6-12  |                        |          |          | 1½ drachms                                   |   |
| 17-6-12  | Electrocardiographic   | 150      | 300      | 1½ drachms                                   | Chiefly 2:1, irregular while resting.   |
| 18-6-12* | Electrocardiographic   | 144      | 288      | Stroph. stopped.<br>(Total<br>dr. xv. m. xx) | Chiefly 2:1, irregular while resting.   |

\*The treatment was abandoned on the 18th, as there seemed little or no prospect of obtaining fibrillation. Diarrhœa had been present for a number of days.

The patient's general condition had improved a good deal, chiefly it may be presumed as a result of rest and the slower ventricular action, whenever he was lying or quiet. During the whole of the treatment he rested in bed or upon a couch, getting up for a few hours each day.

13-9-12. The patient writes that his heart rate is still fast.

Two figures are published from this case. The first (Fig. 28) was taken when the patient first came under observation. It shows a regular auricular action at 324 per minute: the ventricle beating at half this frequency. The auricular complexes are clearly visible in all three leads. In lead *I* they are small, pointed, upwardly directed peaks. The *P-R* interval is of about .09 sec. duration. In leads *II* and *III* the auricular complexes are contiguous, together forming a wavy line. The point which represents the onset of auricular systole in these leads can be ascertained. The quick deflections (*P*) of lead *I*, must be held to mark the commencement of systole (for at the commencement of systole the potentials of right and left side are unbalanced). Taking the same *P-R* intervals for leads *II* and *III*, we arrive at the commencements of the upstrokes. *P*, therefore, is convex in each of these leads and starts in an upstroke. *T* is seen only in lead *I*.

Fig. 29 was taken from the same subject four months later while he was under digitalis. A higher grade of heart-block had developed as a result of the drug administration. The auricular rate is 308. The ventricular action is very irregular, consisting of a mixture of 2:1 and 5:1 ratios. The *P-R* intervals, which vary in length, will be referred to in more detail at a later stage.

*Summary.* In a man of 53 years, attacks of palpitation and rapid heart action had been present for 38 years. When first seen the rapid action had been persistent for three years. An auricular rate which varied between 264 and 324 was recorded and was persistent over a period of observation of five months. The ventricle responded to each second auricular contraction. Posture had no influence on the auricular rate; a continued course of digitalis appeared to reduce it somewhat. Under full doses of digitalis the ventricular rate was retarded, the pulse becoming extremely irregular. The digitalis was withdrawn before fibrillation of the auricles could be induced. Tincture of strophanthus was used and produced similar ventricular slowing. Pressure on the vagus (right and left) produced increased ventricular, but no auricular slowing, while the patient was under the influence of these drugs. The treatment with strophanthus had also to be abandoned. The general condition of the patient at the end of treatment seemed improved.

*CASE 4.* W. T., a traveller, aged 62, came under observation on May the 24th, 1912.

*Past illnesses.* When young he had scarlet fever and smallpox. Until the age of 35 his health remained good; he then had an attack of appendicitis. At the age of 40 he developed a hernia. At 42 he had inflammation of the lungs and a slight attack of typhoid fever. At 45 he developed a fistula and subsequently hæmorrhoids. He was operated upon twice for the rectal conditions and subsequently was not bothered by them.

*History of cardiac condition.* In the late months of the year 1911 he noticed a little shortness of breath on exertion. In the first week of January, 1912, he was laid up with a severe attack of "influenza"; the illness commenced with headache, prostration, cough and fever (100-101° F.); he was in bed for eight weeks and during that time his doctor noticed that his heart began to beat rapidly. The patient noticed nothing the matter with his heart until his attention was drawn



to it. He got up early in March and experienced feebleness and considerable shortness of breath upon exertion. He was easily exhausted and had sharp short pains localised to the left side of his chest. The pains were not influenced by exercise or by food. They came on at any time of the day or night, and often while he was sitting quietly. Usually they lasted but a few minutes. He also suffered from cramping pain and soreness of the left shoulder which usually disturbed him most when in bed; the shoulder pain was present while he was under treatment. Food was always taken well, though he had suffered from slight indigestion at times, and the bowels were generally constipated. The heart's action remained continually rapid.

*Condition on May the 24th, 1912.* A heavily built man with florid countenance, he had a trace of cyanosis. His breath was somewhat short and the slightest exertion enhanced this symptom, so that in walking up a gentle declivity he was obliged to halt every few hundred yards. The limits of cardiac dulness lay  $2\frac{1}{2}$  and  $6\frac{1}{2}$  inches to the right and left of the mid-sternal line, respectively. The heart sounds were natural and there were no murmurs. The heart's action was rapid. The arteries showed no signs of thickening; the systolic blood pressure was 140 mm. Hg. The urine was normal. Neither the liver nor the spleen could be felt. The teeth were carious.

The patient was examined on two occasions before observation became continuous. He was treated first with digitalis and secondly with strophanthus. The observations are embodied in the following tables.

| DATE.   | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS.                            | REMARKS.  |
|---------|------------------------|----------|----------|-----------------------------------|---|
| 19-3-12 | Electrocardiographic   | 138      | 276      | None                              | 2:1 heart-block.  |
| 22-5-12 | Electrocardiographic   | 138      | 276      | None                              | 2:1 heart-block.  |
| 24-5-12 | Polygraphic            | 131      | 262      | Tinct.<br>Digit.<br>m. x          |   |
| 25-5-12 | Polygraphic            | 136      | 272      | m. xxx                            | 2:1 heart-block.  |
| 26-5-12 | Electrocardiographic   | 136      | 272      | m. xxx                            | 2:1 heart-block.  |
| 27-5-12 |                        |          |          | m. xxx                            |   |
| 28-5-12 | Electrocardiographic   | 135      | 270      | m. xlv                            | 2:1 heart-block.  |
| 29-5-12 | Electrocardiographic   | 138      | 276      | m. xlv                            | 2:1 heart-block.  |
| 30-5-12 | Electrocardiographic   | 114-137  | 274      | m. xlv                            | 2:1 with occasional 4:1 periods. A little pain in left chest. Pressure on right vagus slowed ventricle but not auricle. |
| 31-5-12 | Electrocardiographic   | 94       | 278      | m. lx<br>(Total<br>dr. iv, m. lv) | 2:1 and 4:1 mixed.<br>Very irregular.   |

On the 31st the patient commenced to vomit. The digitalis was omitted and, after a few days rest, strophanthus was given.

|        |                      |         |     |                            |   |
|--------|----------------------|---------|-----|----------------------------|---|
| 1-6-12 | Polygraphic          | 100-130 | 260 | None                       | 2:1 with 4:1 periods. In bed, sickness stopped.   |
| 3-6-12 | Polygraphic          | 90-132  | 264 | None                       | Periods of 2:1, also 3:1, 4:1 and 5:1. No sickness or nausea.                             |
| 4-6-12 | Electrocardiographic | 110-134 | 268 | Tinct.<br>Stroph.<br>m. xx | Vagal pressure (right) produced ventricular but not auricular slowing. 2:1 and 4:1 mixed. |
| 5-6-12 | Electrocardiographic | 136     | 272 | m. lx                      | 2:1 heart-block.  |

| DATE.   | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS.  | REMARKS.   |
|---------|------------------------|----------|----------|---|--|
| 6-6-12  | Electrocardiographic   | 100-135  | 270      | Tinct. Stroph. m. lx                                      | Slight diarrhoea and giddiness. 2:1 heart-block. Some 4:1 periods.   |
| 7-6-12  | Electrocardiographic   | 125-135  | 270      | m. lx   | Chiefly 2:1. Some 4:1 periods lying.   |
| 8-6-12  | Pulse counts           | 80-100   |          | m. lx   | Very irregular; in bed.  |
| 9-6-12  |                        |          |          | m. xl   |  |
| 10-6-12 | Polygraphic            | 130      | 260      | m. lx   | 2:1 occasional periods of 4:1. Had just been dressing himself. Pressure on either vagus caused slowing.                                |
| 11-6-12 | Electrocardiographic   | 115-136  | 272      | m. lxx  | Chiefly 2:1, occasional periods of 4:1.  |
| 12-6-12 | Electrocardiographic   | 100-133  | 266      | m. lxxv   | 2:1 with frequent 4:1 periods, especially while resting.   |
| 13-6-12 | Electrocardiographic   | 105-135  | 270      | m. l  | 2:1 with frequent 4:1 periods, especially while resting.   |
| 14-6-12 | Electrocardiographic   | 95-135   | 270      | m. xxv  | 2:1 with frequent 4:1 periods, especially while resting.   |
| 15-6-12 | Electrocardiographic   | 98-134   | 268      | m. l  | 2:1 with frequent 3:1 4:1 and 5:1 periods.   |
| 16-6-12 |                        |          |          | m. lxxv   |  |
| 17-6-12 | Electrocardiograms     | 90       | 275      | m. lxxv   | Very irregular, 2:1, 3:1, 4:1 and 5:1 periods mixed.   |
| 18-6-12 | Electrocardiograms     | 95       | 273      | m. l  | Very irregular, 2:1, 3:1 and 4:1 periods mixed.  |
| 19-6-12 | Electrocardiograms     | 92       | 276      | m. lv   | Very irregular, 2:1, 3:1 and 4:1 periods mixed.  |
| 20-6-12 | Electrocardiograms     | 80       | 270      | m. xxx<br>Stroph.<br>stopped.<br>(Total<br>dr. xv, m. xv) | Very irregular. 3:1 and 4:1 mixed. Diarrhoea has been present since the 6th.   |
| 23-6-12 | Polygraphic            | 132      | 264      | None  | Chiefly 2:1. Occasional 3:1 and 4:1 periods. Diarrhoea stopped. Has improved in general condition. Vagal pressure slows the ventricle. |

23-6-12. On this date the treatment was abandoned as there seemed no prospect of obtaining fibrillation.

|         |                      |     |     |      |   |
|---------|----------------------|-----|-----|------|---|
| 19-7-12 | Polygraphic          | 133 | 266 | None | Pressure on right vagus produced long pauses. |
| 14-8-12 | Electrocardiographic | 136 | 272 | None | Health unaltered.                             |
| 11-9-12 | Electrocardiographic | 135 | 270 | None | Health unaltered.                             |



Observations were made upon the heart rate as affected by posture and exercise. On the 24th of May, 1912, curves were taken from the brachial artery in the standing and lying postures : the pulse was regular throughout, the ventricle beating at half the auricular rate.

| Lying. | Standing. |
|--------|-----------|
| 130    | 130       |
| 130    | 132       |
| 130    | —         |

Similar observations were made upon June the 23rd, 1912.

| Lying. | Standing. |
|--------|-----------|
| 129    | 134       |
| 132    | 134       |
| 130    | 133       |

Similar observations were made on July the 19th, 1912.

| Lying. | Standing. |
|--------|-----------|
| 133    | 132       |
| 132    | 132       |
| 130    | 133       |

On June the 23rd, 1912, two continuous curves were taken immediately after exercise.

Rate before exercise (standing) 134.

Rate each half minute after exercise (standing) 134, 134, 134.

Rate each half minute after exercise (standing) 134, 134, 134, 134.

Another curve of the same sort was taken on July the 19th, 1912.

Rate before exercise (standing) 135.

Rate each half minute after exercise (standing) 135, 134, 136, 137, 137, 137, 136, 136.

The electrocardiograms from this case are very similar to those of *CASE 3*. The two published curves (Fig. 30 and 31) were taken within two days of each other, the second (Fig. 31) shows the first reaction of the heart to digitalis. In Fig. 30 the ratio is as 2 : 1, the auricular rate being 276 per minute. *P* is not clear in lead *I*, but in leads *II* and *III* the continuous line of auricular complexes has a form almost identical with that seen in Fig. 19 and 20 ; but there is a difference. In Fig. 20 similar phases of the wavy lines correspond in leads *II* and *III* ; while in Fig. 30, the upstroke of each wave in lead *II* corresponds to a point a little to the right of the upstroke in lead *III*. *T* appears in lead *I* only.

The irregular heart action of Fig. 31 consists of responses to each second, third or fourth auricular systole ; there is as usual a variation in the length of the *P-R* interval, according as it falls after a long or short ventricular cycle.

*Summary.* A man of 62 years developed a continuously rapid heart action during a severe attack of "influenza." The auricular rate was 270, the ventricular rate 135 per minute. After the auricular "flutter" had been present for five months, he was treated first with digitalis and secondly with strophanthus. These drugs slowed the ventricle but had no influence upon the auricle. Vagal (right and left) pressure, while he was under the influence of both these drugs caused further ventricular slowing without affecting the rate of the auricle. Posture influenced the rate of the auricle but a few beats per minute ; exercise had no effect. The treatment with both digitalis and strophanthus was abandoned ; fibrillation could not be obtained. There was slight but definite improvement in the condition, presumably as the result of the rest and drug administration.

## CASE 5.\* W. G., a French polisher, 60 years of age.

*Past history.* The patient had gonorrhœa at the age of 17. At 23 he was laid up with some obscure chest ailment.

*History of cardiac condition.* There had been periodic attacks of breathlessness of a distressing and exhausting character for three and a half months.

*Condition, November the 9th, 1911.* Orthopnoea and slight cyanosis were present. The pulse was constantly rapid and regular. The apex beat lay in the fifth and sixth spaces; the limits of heart dulness were  $1\frac{1}{2}$  and 6 inches to right and left of the mid-sternal line. A systolic murmur was heard at the apex. The liver was enlarged; the urine was normal. The blood pressure varied between 116 and 120 mm. Hg.

The mechanisms and the rates of heart beat are summarised in the following table which shows the course of the illness under treatment.

| DATE.                      | METHOD OF EXAMINATION. | Vs RATE.       | As RATE. | DRUGS.                      | REMARKS.  |
|----------------------------|------------------------|----------------|----------|-----------------------------|---|
| 19-11-11<br>to<br>25-11-11 | Pulse counts           | 145-150        |          | None                        | In all probability 2:1 heart-block throughout.  |
| 25-11-11                   | Pulse count            | 150            |          | Digit.<br>infus.<br>dr. xii | 2:1 heart-block. The rate was not changed by posture.   |
| 26-11-11                   | Electrocardiographic   | 146.5          | 293      | dr. xii                     | 2:1 heart-block. Occasional premature beats from the ventricle.   |
| 28-11-11                   | Electrocardiographic   | 150            | 300      | dr. xii                     | 2:1 heart-block.  |
| 1-12-11                    | Electrocardiographic   | 74.8-<br>149.5 | 299      | dr. xii                     | 2:1 heart-block with occasional 4:1 periods.  |
| 2-12-11                    | Electrocardiographic   | 72-100         | 288      | dr. xii                     | 4:1 heart-block with occasional 2:1 periods.  |
| 3-12-11                    | Polygraphic            | 73             | 292      | dr. xii                     | 4:1 heart-block.  |
| 4-12-11                    | Electrocardiographic   | 72             | 288      | dr. xii                     | 4:1 heart-block. Pressure on either carotid sheath gave further slowing of the ventricle but none of the auricle. |

The condition remained unaltered until December the 11th, 1911.

|          |                      |    |   |                                 |  |
|----------|----------------------|----|---|---------------------------------|--|
| 11-12-11 | Electrocardiographic | 44 | 0 | Digit.<br>infus.<br>dr. xii     | Gross irregularity. Auricular fibrillation.                    |
| 12-12-11 | Polygraphic          | 46 | 0 | dr. xii<br>(Total<br>xxvii oz.) | Gross irregularity. Auricular fibrillation. Digitalis stopped. |
| 13-12-11 | Polygraphic          | 45 | 0 | None                            | Auricular fibrillation.  |
| 14-12-11 | Polygraphic          | 56 | 0 | None                            | Auricular fibrillation.  |
| 18-12-11 | Polygraphic          | 53 | 0 | None                            | Auricular fibrillation.  |
| 20-12-11 | Polygraphic          | 62 | 0 | None                            | Auricular fibrillation.  |

\* This case has been fully reported in *Heart*, 1912, III, 285. I repeat the chief facts of the case in the form of a summary, and enter the case in this section of the communication because I am able to add to the first report.



| DATE.  | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS. | REMARKS.  |
|--------|------------------------|----------|----------|--------|---|
| 4-1-12 | Electrocardiographic   | 63       | 63       | None   | Normal rhythm. Occasional premature auricular contractions. |
| 6-1-12 | Electrocardiographic   | 63       | 63       | None   | Normal rhythm. Occasional premature auricular contractions. |

8-1-12. Discharged from hospital, much improved : colour good, no liver enlargement, breathing free and easy.

|         |                      |        |     |      |   |
|---------|----------------------|--------|-----|------|---|
| 20-1-12 | Electrocardiographic | 82     | 82  | None | Normal rhythm. Pressure on neither carotid sheath had any effect. |
| 24-2-12 | Electrocardiographic | 132    | 264 | None | Has been feeling bad again for a week. 2 : 1 heart-block present. |
| 27-4-12 | Electrocardiographic | 68-136 | 272 | ?    | Chiefly 2 : 1 heart-block. A good many 4 : 1 periods.             |

Re-admitted to hospital 18-5-12, complaining of pain in the chest, shortness of breath, palpitation and swelling of the abdomen and feet. The pulse was continuously rapid. Slight cyanosis, dyspnoea, liver enlargement, ascites and dropsy of the feet were present.

|         |                      |        |     |  |  |
|---------|----------------------|--------|-----|--|--|
| 18-5-12 | Pulse counts         | 145    |     | Inf. dig.<br>dr. xii daily             |  |
| 22-5-12 | Electrocardiographic | 69-138 | 276 | dr. xii                                | Chiefly 4 : 1 heart-block, some 2 : 1 periods.   |
| 29-5-12 | Electrocardiographic | 72-144 | 288 | dr. xii                                | Chiefly 4 : 1 heart-block, 2 : 1 periods after effort.   |
| 1-6-12  | Electrocardiographic | 64-90  | 256 | dr. xii                                | Chiefly 4 : 1 heart-block, some 2 : 1 and 3 : 1 periods. Pressure on either vagus produced further slowing.    |
| 5-6-12  | Pulse count          | 67     |     | dr. xii                                | The pain has gone, and all the signs of liver enlargement. Ascites and dropsy have disappeared. Pulse regular. |
| 6-6-12  | Pulse count          | 60     |     | dr. xviii daily                        | Pulse regular.   |
| 9-6-12  | Polygraphic          | 62     | 248 | dr. xvii daily.                        | 4 : 1 heart-block.   |
| 15-6-12 | Polygraphic          | 58-64  | 256 | dr. xviii daily                        | Chiefly 4 : 1 heart-block, some 8 : 1 periods; pressure on either vagus produced further slowing.              |
| 20-6-12 | Polygraphic          | 54-62  | 248 | Digit.<br>stopped.<br>(Total lxii oz.) | Chiefly 4 : 1 heart-block, some 6 : 1 and 8 : 1 periods.   |

| DATE.                             | METHOD OF EXAMINATION. | Vs RATE. | As RATE. | DRUGS. | REMARKS.   |
|-----------------------------------|------------------------|----------|----------|--------|--|
| 24-1-12                           | Pulse counts           | 80-110   |          | None   | Very irregular.  |
| 27-6-12                           | Electrocardiographic   | 62.5-125 | 250      | None   | General condition very much improved. Pressure on vagi still induces ventricular slowing. While the patient is lying the ratio is 4 : 1 ; after exercise it is 2 : 1 or irregular. |
| 27-6-12 Discharged from hospital. |                        |          |          |        |  |
| 6-7-12                            | Electrocardiographic   | 95       | 0        | None   | Auricular fibrillation.  |
| 3-8-12                            | Electrocardiographic   | 85-120   | 85-120   | None   | Normal rhythm. Pressure on right and left vagi produced great slowing of whole heart, with slight prolongation of <i>P-R</i> interval.   |
| 14-9-12                           | Electrocardiographic   | 65       | 65       | None   | Normal rhythm. Occasional premature auricular contractions.  |

Observations were made as to the effect of posture on the auricular rate (calculated from the regular ventricular rhythm) in this case on a number of occasions. The effect was always negative or inappreciable. An example of readings may be given :—

| Lying. | Standing. |
|--------|-----------|
| 249    | 250       |
| 249    | 248       |
| 251    | 245       |
| 249    | 246       |

Exercise, similarly, was without appreciable result. Before exercise the auricular rate was 246, at half-minute intervals, directly after exercise, the readings were 244, 246, 245 and 252 ; after further exercise, they were 256, 254, 254 over intervals of one minute.

Control curves were taken on September the 3rd, while the mechanism was normal. The rate (auricle and ventricle) before exercise was 75, after exercise 110 and later 80. Postural effects were also observed.

| Lying. | Standing. |
|--------|-----------|
| 84     | 111       |
| 79     | 110       |
| 82     | 112       |
| 84     | 111       |

The electrocardiograms of this case were fully illustrated in my former paper. The *P* summits of the periods of flutter were clear in all leads ; and those of lead *I* were small, pointed and upright summits. In leads *II* and *III* the lines of auricular waves were contiguous, the separate summits being convex ; the rate was about 300 per minute.

Curves showing, chronologically, mixed 2 : 1 and 4 : 1 periods, regular 4 : 1 block ; auricular fibrillation ; and lastly, the normal rhythm were published. The changes occurred as a result of digitalis administration. The auricular oscillations were more conspicuous during the period of flutter than during the period of fibrillation. The *P* summits of the normal rhythm were quite unlike those of the period of flutter. The shape of the initial



ventricular deflections remained unchanged throughout. *T* was scarcely visible in any lead.

*Summary.* A man of 60 years developed a continuously rapid heart action. The auricular rate was 300, the ventricular 150. After the "flutter" had been present for some while, he was treated with digitalis. This drug slowed the ventricle to a fourth of the auricular rate. During this stage, pressure on either vagus caused further slowing of the ventricle but had no effect upon the auricular rate. Eventually fibrillation appeared and, the digitalis being stopped, the normal rhythm reappeared. Some seven weeks later the flutter came again and digitalis, though it produced conspicuous slowing, seemed to have no influence upon the auricles. Eventually he was discharged and a week later fibrillation was found; this subsided and the normal rhythm was again restored. The flutter rate was influenced by posture or exertion to no appreciable extent; the normal rhythm, when present, was influenced by both, and vagal pressure (right and left) gave slowing, during this stage.

#### CASE 6. F. T., an actor of 47 years.

On June the 18th, 1912, Dr. Jordan, of Guy's Hospital, asked me to examine a case of tachycardia. The patient had been to Dr. Jordan in the morning for an examination of the alimentary canal. Looking at the heart upon the fluorescent screen, Dr. Jordan could see an extremely rapid undulation of the heart margin; the systolic displacement of the ventricular border was almost absent, a tremulous movement of the left outline was alone visible. At the time, the pulse was practically imperceptible.

In the evening I saw the patient at Dr. Jordan's rooms. He seemed in no distress, the breathing was free. The ventricular action was quite regular, the rate being about 160 per minute. The pulse was also regular and fairly full. The systolic displacement of the left heart border was clearly visible on the fluorescent screen and amounted to  $\frac{1}{4}$  or  $\frac{1}{2}$  an inch. The tug of the ventricle upon the right auricle was clear, but no intrinsic beating could be seen in this auricle. On the other side, in the position of the left appendix, there was a movement of much greater rapidity. The arch of the aorta showed slight senile dilatation. The heart limits to percussion and as seen upon the screen were a little wide towards the left side. There were no murmurs. The arteries seemed soft and the tension moderate. The same evening electrocardiograms were taken. The patient gave a history of attacks of palpitation coming on suddenly and being accompanied by rapid heart action ever since he was a young man. The attacks had left him exhausted and unfit for exertion. They were brought on by exercise or emotion; he had had them while on the stage, but had always managed to complete his evening's work, though often only with considerable effort. For years he had suffered from attacks of acute gout in the feet and wrists, the joints becoming inflamed, swollen and tender. The condition moved from joint to joint with suddenness. There were no tophi in the ears, but chronic changes were found in the metatarsophalangeal joints of the great toes and in the wrists. The patient refused treatment.

The electrocardiograms showed an extremely rapid auricular action, the rate being 330. The ventricle was beating at half this rate. The electrocardiograms are shown in Fig. 32. *T* is present in leads *I* and *II* but not in lead *III*. The auricular summits in lead *I* are small and inconspicuous, though visible. In leads *II* and *III* they are of the usual form, and are contiguous. (Compare Fig. 29 and 31.) It is probable, but not certain, that each auricular cycle commences with an upstroke.

*Summary.* A man of 47 years had suffered since he was a young man from attacks of rapid heart action. He suffered also from gout. He was

seen on one occasion only; the auricles were found to be beating at 330 per minute and the ventricles at 165 per minute. It is probable that on occasions the ventricular action responded more rapidly; in other words that the grade of 2:1 heart-block gave place to one in which the responses were successive.

*CASE 7.* A. P., an elderly gentleman, was examined electrocardiographically only and I have notes neither of his symptoms nor of the size of the heart or its auscultatory signs. The electrocardiograms are shown in Fig. 33. The heart's action is quite regular. The auricular rate is 228, the ventricular rate 114. 2:1 heart-block is present. The auricular summits are most distinct in lead *II*, but are also clearly visible in leads *I* and *III*. In all leads the summits are upright. The curves differ from the others of this series in that the *P* summits are not contiguous; distinct intervals are present between the termination of the downstrokes and the commencement of upstrokes. This fact is probably accounted for by the slow rate of auricular action as compared with that found in other cases. The heart action was a persistent one, having been present for some months.

*CASE 8.* W., a clergyman of 52 years, was seen on a single occasion and for electrocardiographic examination only.

I have but brief notes of his history. For some while he had suffered from breathlessness and a sense of weakness and exhaustion whenever he exerted himself. He was unable to walk fast, though with effort he could manage to keep going for a good many miles. He had been treated for albuminuria some years before and was reported cured. There was some cardiac enlargement to the left, but no murmurs; the heart action was very irregular.

The electrocardiograms showed that the auricle was beating regularly at 260 per minute. The ventricular rate varied between 90 and 130. As a rule the ventricle responded to each alternate auricular contraction; 3:1 and 4:1 periods occurred from time to time. The ventricular complexes were very similar to those seen in the other patients. In leads *II* and *III* the auricular complexes were contiguous and were of the customary form, forming as a whole a zig-zag line, composed of short steep upward deflections and longer and more inclined downward deflections. The type of curve is shown in Fig. 29. The summit *T* could not be found in any lead.

#### *Previously reported cases.*

*CASE 9.* (Reported by Hertz and Goodhart.<sup>1</sup>) A woman of 39 years.

There was a history of scarlet fever at the age of 11, after which she suffered from palpitation; for this she was treated eight years later and became perfectly well. A few months before she was examined she became breathless and developed lividity. The heart beat irregularly at this time.

The patient had an organic hemiplegia. There was but little cardiac enlargement, a systolic apical murmur was present, the rate of beat was slow. At times a presystolic or early diastolic murmur was heard. The ventricular beats were coupled. On digitalis the ventricular rate fell and reached 44 beats per minute.



Polygraphic curves showed an auricular action varying between 216 and 234 beats per minute. Atropine and exercise had no effect on the auricular rate but increased the ventricular rate. A high grade of partial heart-block is shown in the single curve illustrating the case. She was under observation for nearly a year and the auricular action was constantly fast over this period.

*CASE 10.* (Reported by Jolly and Ritchie,<sup>2</sup> *CASE 1*). A man of 61 years.

The ventricular action was always slow, varying between 30 and 63 beats per minute, the usual rate being in the neighbourhood of 33 beats per minute. He had suffered from complete heart-block, the auricle and ventricle beating independently at the usual rates found in such cases, and in addition, attacks of great acceleration of the auricle were observed, the last of which became permanent and was watched for two years. The auricular rate, while it was accelerated, varied between 234 and 300 per minute. The only symptoms mentioned were those of Adams-Stokes' syndrome. Electrocardiograms and polygraphic curves are given; they show complete block and an extremely fast auricular action. The type of auricular curve was almost identical with that shown in Fig. 29 of this paper. Digitalis apparently was not used. Atropine was given and had no influence upon the auricular and ventricular rates.

*CASE 11.* (Reported by Rihl,<sup>9</sup> *CASE 1*.) A cabinet maker of 55 years.

The patient was said to have suffered from typhoid at 18 and pneumonia a year later. For many years afterwards he had painful swellings of single joints of a few days duration. He gave a history of four months palpitation and breathlessness, which were especially prominent after exertion.

The apex beat was in the fifth and sixth spaces. The left border of dulness lay a finger's breadth outside the medio-clavicular line; the right border at the left edge of the sternum. The blood pressure was 86-124 mm. Hg. There were no murmurs. Some of the arteries were tortuous. The progress of the case is summarised in the following table.

| DATE.  | METHOD OF EXAMINATION. | Vs RATE. | As RATE.         | DRUGS.          | REMARKS.  |
|--------|------------------------|----------|------------------|-----------------|---|
| 2-6-10 | Polygraphic            | 143-150  | Probably 246-300 | None            |   |
| 5-6-10 |                        |          |                  | Digalen m. xvii |   |
| 6-6-10 | ?                      | 150      | Probably 300     | m. l            |   |
| 7-6-10 | Polygraphic            | 100      | Probably 290     | m. xxxiv        | Heart action irregular. 2:1 and 4:1 periods.          |
| 8-6-10 | Polygraphic            | About 85 | Probably 304     | m. xxxiv        | Heart action irregular. 4:1 with 2:1 and 3:1 periods. |

| DATE.   | METHOD OF EXAMINATION. | <i>Vs</i> RATE. | <i>As</i> RATE. | DRUGS.                                     | REMARKS.   |
|---------|------------------------|-----------------|-----------------|--|--|
| 9-6-10  |                        |                 |                 | m. xxxiv                                   |  |
| 10-6-10 |                        |                 |                 | m. xxxiv                                   |  |
| 11-6-10 | Polygraphic            | About<br>74     | About<br>296    | m. xxxiv<br>(.0006 gr.<br>Atropine)        | Atropine injection temporarily restored original condition. Rates 140 and 280. |
| 12-6-10 |                        |                 |                 | m. xxxiv                                   |  |
| 13-6-10 | ?                      | 76              |                 | m. xxxiv                                   | Irregularities infrequent. Probably chiefly 4 : 1.                             |
| 18-6-10 |                        |                 |                 |  | Systolic murmur audible at apex.   |
| 23-6-10 | ?                      | Approx.<br>100  |                 |  | Very irregular again.  |
| 24-6-10 | Polygraphic            | Approx.<br>95   | Approx.<br>288  | Atropine<br>.001 gr.<br>Digalen<br>m. xvii | Atropine restored original 2 : 1 rhythm. (Rates 141 and 282).                  |
| 25-6-10 |                        |                 |                 | m. l                                       |  |
| 26-6-10 | ?                      | Approx.<br>75   |                 | m. l                                       | Irregularity infrequent.   |

Rihl gives electrocardiograms and polygraphic curves which are characteristic of the condition. The auricular curves are almost identical with those seen in Fig. 29 of this paper. The *P-R* intervals are similar. The auricular representative commences with an upstroke in leads *II* and *III*, and are not, as Rihl states, inverted. *T* is clearly visible in lead *I* only.

To sum up, the case was one in which tachycardia had probably been present for four months; the ventricular rate was 143-150; the auricular rate was 286-300. Digalen reduced the ventricular but not the auricular rate and led to irregularity and slowing of the pulse. Atropine abolished this digitalis effect. Pressure on the vagus increased it but did not alter the auricular rate.

*CASE 12.* (Rihl,<sup>9</sup> *CASE 2*.) A widow of 32 years and a waitress.

At 24 years she had typhoid and pneumonia. Two years later her knees were swollen. Palpitation and dyspnoea, especially after strenuous exercise, had been present for a year; for four weeks the feet had been swollen. The apex beat lay in the sixth interspace in the anterior axillary line. No extension of dulness could be found to the right of the sternum; the left border lay beyond the mid-clavicular line. A conspicuous thrill was felt at the apex and two murmurs were heard. The urine flow was not free. The blood pressure lay between 92 and 112 mm. Hg.

Polygraphic curves showed an auricular rate of 206-222. The ventricular rate varied, being sometimes half the auricular, the pulse then being regular, or sometimes less, the pulse being then usually irregular. Digitalis gave



rise to ventricular slowing and irregularity. Vagal pressure increased the block, but whether the heart was under digitalis at the time is uncertain. The patient was under observation from time to time for a period of 18 months and the fast auricular action seems to have been present during the whole of this period.

*CASE 13. (Rihl,<sup>9</sup> CASE 3.) A labourer of 72 years.*

A year before coming under observation he suddenly became afflicted with palpitation and developed cough and swelling of the legs. The symptoms disappeared after a long stay in hospital. For three weeks before admission he had had the same symptoms.

The apex beat lay in the sixth space. The heart dulness was considerably increased to the left. There was no murmur. The blood pressure lay between 145 and 200 mm. Hg.

The case was examined by means of polygraph curves. The ventricular rate was half the auricular, the latter being between 200 and 214 per minute. The ventricular responses were sometimes slower and irregular. Digitalis increased the grade of heart-block. So also did vagus compression, but it is not clear whether the heart was under the influence of digitalis at the time. On three occasions curves were taken which showed what seems to have been fibrillation of the auricles. The change apparently did not result from digitalis administration. The ventricular rate was then 120 or less.

*Three cases in which the condition was not recognised.*

*CASE 14. (Reported by Mackenzie,<sup>8</sup> CASE 37; the curves were fully interpreted by the writer at a later date.<sup>7</sup>) An army official, aged 47, who gave no history of past illnesses.*

*History of heart condition.* For eight years he had suffered from attacks of palpitation. For three years they were not accompanied by much distress; after that time he had a number of attacks and had to rest. After an interval of several years of freedom from them they returned, and when seen he had been suffering from attacks of much greater severity, accompanied as they were by great exhaustion and prostration.

*Condition on May the 3rd, 1910.* Cyanosis and orthopnoea were present. The pulse was soft and regular, the rate being 140; the blood pressure was 140 mm. Hg. The heart's dulness lay 0 and 4½ inches to the right and left of the mid-sternal line. There were no murmurs.

*Progress.* For five weeks the ventricular rate was maintained, lying usually between 130 and 150, but rising on occasion to a rate of 290 and 300. On July the 22nd, or about eleven weeks after admission, the pulse remaining rapid, he was given tincture of digitalis in doses of 20 minims three times a day. Five days later the pulse rate dropped to 55 and the ventricular action became very irregular, though there were still occasional rapid and regular paroxysms. On the 28th, periods of normal rhythm and irregular heart action succeeded each other. On this day the digitalis was stopped but was resumed on the 30th and continued till August the 7th in half doses. Irregular action was present from the 2nd till the 10th of August. From August the 17th to the 24th, normal rhythm, regular tachycardia and irregular action occurred from time to time. After the 24th the regular tachycardia became more frequent and digitalis was again given on September the 4th in doses of 5 minims three times a day and later 10 minims a day. Under this régime the tachycardia gradually disappeared; after the 29th it was not seen.

*Summary.* It may be said that the patient suffered from attacks of a curious form of regular tachycardia, which gave place under digitalis to a slow irregular action, and that finally the normal rhythm was restored, the auricle and ventricle beating at the same rates. Electrocardiograms taken during the periods of regular tachycardia showed a ventricular rate of 160

per minute and an auricular action of 320 per minute. The auricular curves were very similar to those shown in Fig. 29 of the present paper. Each commenced with an upstroke. *T* was present in lead *I* only. Electrocardiograms taken during the normal periods showed similar ventricular electric complexes, but the auricular complexes were very different from those of the period of flutter. The polygraphic curves published of the slow irregular action indicate the probable appearance of auricular fibrillation from time to time.

*CASE 15.* (Reported by Turnbull.<sup>11</sup>) A retired medical practitioner aged 74.

The patient gave a history of no previous illness; he had been a healthy and athletic man; he stated that he awoke one morning in January, 1910, feeling ill. His doctor found a rapid ventricular action, and advised rest, but the patient continued his usual occupations, until increasing breathlessness compelled him to lie up. The regular and rapid ventricular action continued for four months. He was treated with digitalis, 20 minims being given three times a day. After seven days treatment a change was noticed in the heart action; it became slow and irregular (probably as a result of increased heart-block). In the venous curves, taken at this time, certain additional waves the meaning of which was obscure at that time (Fig. 1 and 2 of the original paper) were observed. Later the regular tachycardia was re-established. Irregular action again appeared and strips of curve (Fig. 7 of the original paper) showing fibrillation were obtained. Eventually the normal rhythm was restored. Electrocardiograms were published showing the action during the regular and fast periods and also of the restored normal rhythm. I may add that I have recently taken curves from the same subject (June, 1912) and that the normal rhythm has been maintained.

If Turnbull's paper is referred to and the tracings are compared with those of the present communication, it will be obvious that the condition dealt with was one of auricular flutter. In the original paper, I interpret Fig. 1 *a* and *b*, 3 and 4 as showing periods of regular ventricular acceleration with an auricular rate which is exactly double. All the venous waves in Fig. 3 and 4 are auricular. The irregular periods of Fig. 1 *a* and *b*, and Fig. 2 and 6, are I think undoubted examples of irregular response to an auricle whose regular and accelerated beating is maintained. This new interpretation entirely accounts for the additional waves in the venous curves which were so puzzling to Turnbull. Fig. 7 is almost certainly an example of auricular fibrillation.

The electrocardiograms which accompanied the report could not be satisfactorily interpreted at the time, but I think that now the interpretation is clear. I republish the figure as Fig. 34 of this paper and have rearranged the figure and have marked the outline of the auricular representatives on the curve. They are of similar forms to those shown in the other cases now reported, though much more difficult to distinguish. They probably commence in upstrokes as in the other cases.

The upstroke of the auricular beat which commences during a *QRS* phase, almost coincides with the upstroke of *S* in leads *II* and *III*, as now indicated by the dotted lines. The *P* summits of the normal rhythm were quite dissimilar. During the flutter period, *T* is present in lead *I*, but hardly discernible in leads *II* and *III*.



We may summarise Turnbull's case as follows :—The patient had suffered from a condition in which the ventricle beat at 140-150 per minute, the auricle at 280-300 per minute, for four months. As a result of digitalis administration a further and irregular grade of heart-block was established ; subsequently auricular fibrillation appeared, and eventually the normal rhythm was restored and has been maintained for two years.

*CASE 16.\** (Reported by the writer in conjunction with H. G. Schleiter,<sup>5</sup> *CASE 1*.) A cabinet maker of 28 years, came under observation on a number of separate occasions.

*Past illnesses.* There had been no previous illness, except measles as a child and occasional colds.

*History of cardiac condition* (November the 11th, 1910). The first attack was in 1908, and from that time on he was subject to them every few months. The attacks were accompanied by palpitation, breathlessness, fainting, fatigue, salivation, sweating, sickness and great prostration.

*Condition between attacks.* A well-built man of healthy aspect. The cardiac limits were normal to percussion : there was a short systolic thrill and murmur, otherwise the heart sounds were normal. The arteries showed a little thickening. The blood pressure lay between 70 and 120 mm. Hg. There were no other physical signs.

*The attacks*, a number of which were closely observed, consisted almost always of paroxysms of auricular fibrillation. On one occasion a paroxysm of regular tachycardia of twelve hours duration was observed. A similar mechanism was observed on a second occasion at the end of a paroxysm which started as auricular fibrillation and lasted for three and a half days. Electrocardiograms of the three states, *i.e.* normal rhythm, regular tachycardia, and auricular fibrillation were published in the original account of this case. The interpretation of the curves showing regular tachycardia have now to be revised in the light of more recent observations. It has become apparent that though the interpretation is correct in so far as it has proceeded, yet an additional auricular systole has passed unnoticed in each ventricular cycle. I republish the curve as Fig. 35 in the present paper. The auricular action is especially well seen in the third lead. As a whole the auricular curves, which have been dotted, are very similar to those of most of the other cases of the series. *P* probably commences in an upstroke. The *P* summits in electrocardiograms from the normal periods were quite dissimilar. *T* was visible in lead *I*, but only just seen in lead *II* and absent in lead *III*. The ventricular rate is approximately 140, the auricular rate is approximately 280. This case is especially noteworthy because the “flutter” of the auricle was transient ; because the auricular fibrillation passed into “flutter” and because it ended spontaneously. The case also illustrates the difficulty of recognising the mechanism, when the ventricle responds to each second auricular beat ; the interpretation was impossible until other cases showing 4 : 1 periods were published.

---

\* Since these pages were written I have seen a report by Josué and Chevallier (Bull. c. Mém. d. l Soc. méd. d. Hôp., Dec. 1911. It was probably of the same nature as those here described.

*The arterial curves.*

A full description of the arterial curves which accompany auricular flutter is desirable ; close examination of them often enables the diagnosis of the condition, and in all cases a great deal may be learnt from them.

I base the statements in this section of the paper upon a detailed analysis of a very large collection of curves, and use a few selected curves for illustration of the chief facts. The correctness of the analysis has been substantiated by electrocardiograms taken from the same case and usually upon the same days ; on a number of occasions simultaneous arterial and electrocardiographic curves have been taken.

To appreciate fully the form and spacing of the arterial beats it is necessary that certain facts should be borne in mind.

1. High rates of ventricular action are often accompanied, where there is degeneration of the myocardium, by *pulsus alternans*. Alternation is evident in the arterial curves of auricular flutter and confuses the analysis.

2. The strength of arterial beats is materially influenced by the pauses which precede them. This is a statement which requires qualification. When we deal with cases of partial heart-block in which the auricular rates are normal and the pulse is irregular, it is customary to find that the arterial beats are of equal heights. All the pauses are of sufficient length to allow the ventricular contractions to be of maximal efficiency. It so happens that when we study the arterial curves of ordinary heart-block, little or no variation in the height of pulse beats is perceived. The arterial curves of auricular flutter, on the other hand, conform to the general rule, when the responses are rapid. Pulse beats which follow 2:1 periods are almost always weak. They resemble extrasystoles. We might modify our original formula, and embody it in a statement which is generally and uniformly applicable. In any given case, pauses of less than a given interval of time are followed by pulse beats which are relatively weak, and the weakness of the beats is evident, be the cause of the shortened pauses what it may.

3. The heart-block in auricular flutter is accompanied, as heart-block often is, by considerable variation of the *As-Vs* intervals ; whereby the expected relation between the lengths of long and short cycles is modified. A long cycle is succeeded by a shortened conduction interval ; a short cycle by a lengthened conduction interval. The beat, which is preceded by a short pause, is small, as I have said ; therefore, the small beats or those which are least effective,\* are the ones before which a long *As-Vs* interval may be conjectured.

---

\* In speaking of less effective ventricular contractions I wish to avoid the controversy as to whether the arterial beat is weak because the contractility of the ventricle is smaller, or whether, on account of the shorter pause, there is lessened ventricular filling. I speak of a less effective ventricular beat simply in the sense that it has less effect on the arterial pressure.



4. The arterial pulse beats which are weak often have a relatively long presphygmic interval; they correspond to ventricular contractions which, as I have said, are already delayed. The delay in the ventricle is exaggerated in pulse curves and is consequently considerable.\*

In the following paragraphs I shall refer again and more explicitly to these factors in describing certain forms of pulse irregularity.

In auricular flutter the pulse rhythm is often perfectly regular for long periods. This occurs, as in Jolly and Ritchie's case, when complete heart-block is present. The pulse is then slow. It also occurs, and far more commonly, when there is a uniform grade of partial heart-block. If the ventricle responds to each fourth auricular contraction, and the auricular rate is from 240 to 300 per minute, then the ventricle is beating regularly and has a rate of from 60 to 75 per minute (see Fig. 11 and 12). When a patient who is in this state is examined by ordinary methods, the true condition of the heart will always pass unnoticed. But the condition is an unstable one, and it may be suspected or recognised, because with exercise the pulse becomes either very irregular, or because it shows exact doubling of rate. The irregularity or doubling is due to a decrease of the block. The pulse becomes irregular when the 4 : 1 periods are mixed with 2 : 1 periods. Doubling occurs when a 4 : 1 ratio gives place to a 2 : 1 ratio. If the ventricle beats in response to each second auricular contraction, it beats regularly and its rate is from 120 to 150 (see Fig. 8 and 9). When the rate is so fast it often happens that alternation is present, and this is especially the case when a 2 : 1 rhythm† follows a long pulse pause (Fig. 6).

The most confusing curves are those in which the responses to auricular systoles occur *irregularly*. We may commence by considering relatively simple examples. Fig. 3 shows a period of 4 : 1 heart-block, interrupted by a single period in which there is a 2 : 1 ratio. I have marked with an asterisk the beat which occurs too early. The cycle which precedes it corresponds to two auricular systoles, that which succeeds it to four. Yet the latter is shorter than the regular 4 : 1 periods; and this helps to distinguish the beat from a true premature contraction or extrasystole. The disturbance is known to result from heart-block because the bracketed stretches of curve are exactly equal. The two shorter cycles are exactly equal to  $1\frac{1}{2}$  cycles of the regular rhythm; each of the bracketed stretches corresponds to six auricular systoles. The 2 : 1 period of the disturbed stretch is shorter than might be expected, and the 4 : 1 period of the same stretch is longer than might be expected, because the weak pulse beat is delayed; and it is delayed because the corresponding *As-V's* interval is relatively long.

---

\* Rihl has also referred to these changes at intervals. They are specially well seen in Fig. 36 and 37.

† In the accompanying figures, the actual ratio of the auricular to ventricular rate is marked above the individual pulse beats.

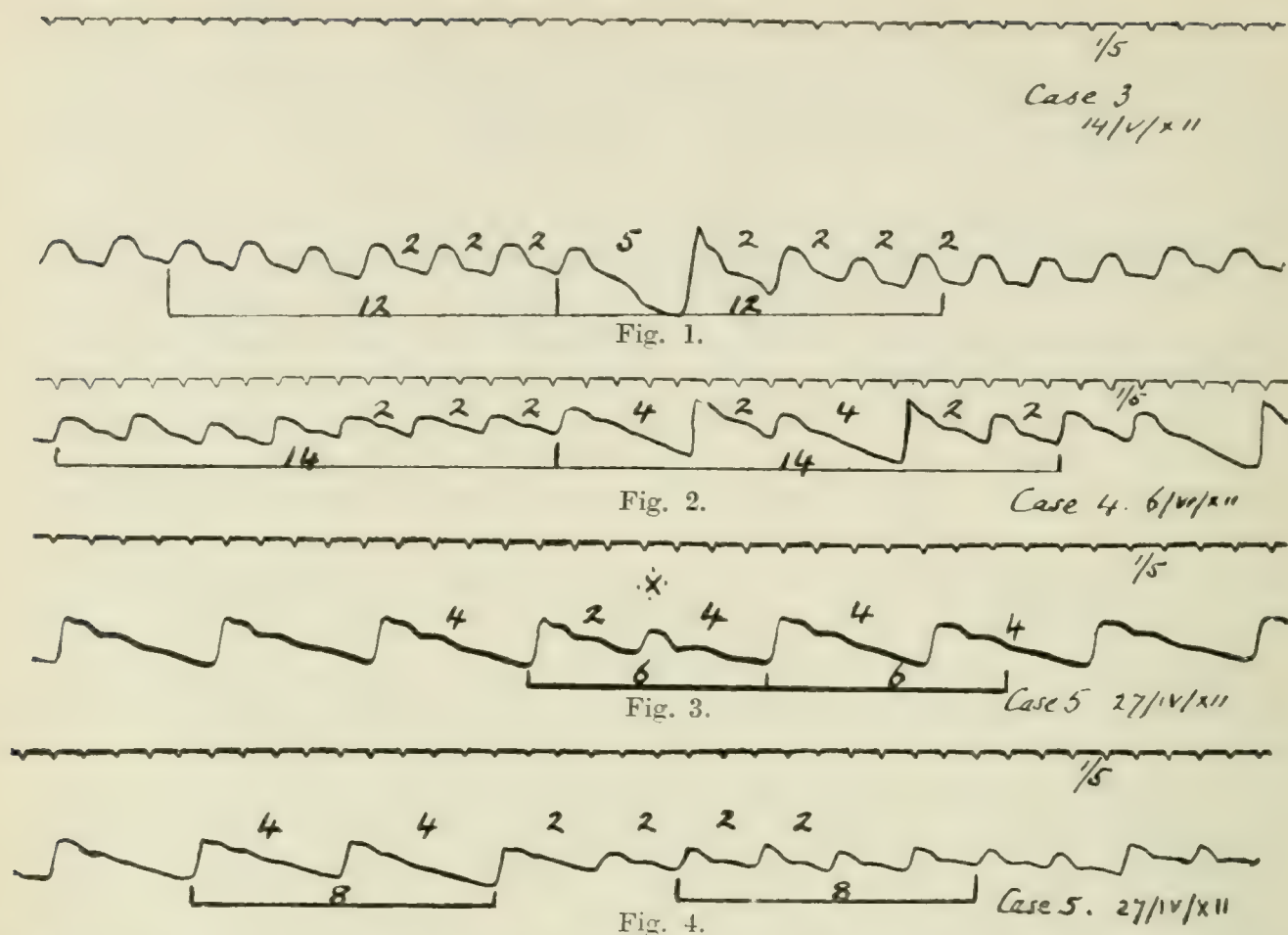


Fig. 1-4. Four arterial curves from cases of auricular flutter. They are published to show the methods adopted in analyses of these curves. The number of auricular cycles to the ventricular cycle is marked above the respective pulse beat. The bracketed portions of any single curve are of equal length: the number of auricular systoles corresponding to the beats included in a bracket is marked on the bracket.

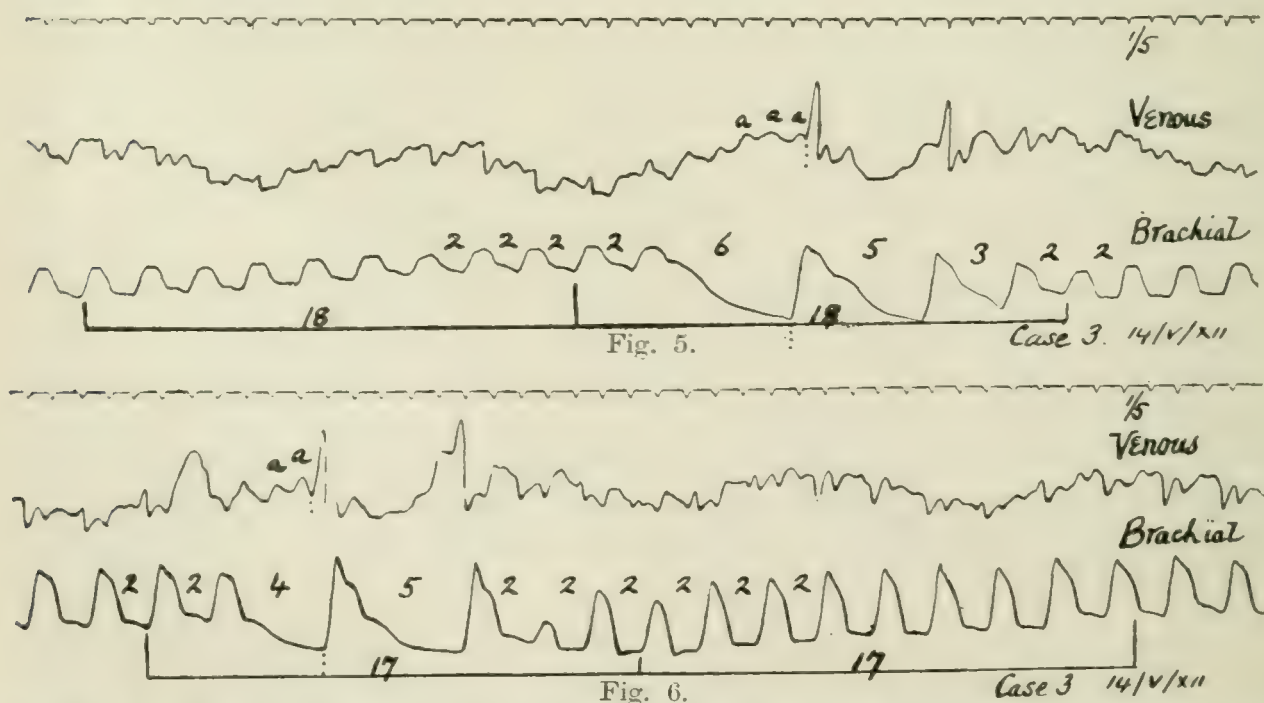


Fig. 5 and 6. Two polygraphic tracings showing arterial and venous curves, taken while the auricles were fluttering. They are published to show the methods of analysis as applied to arterial curves, and the general form of the venous curves.



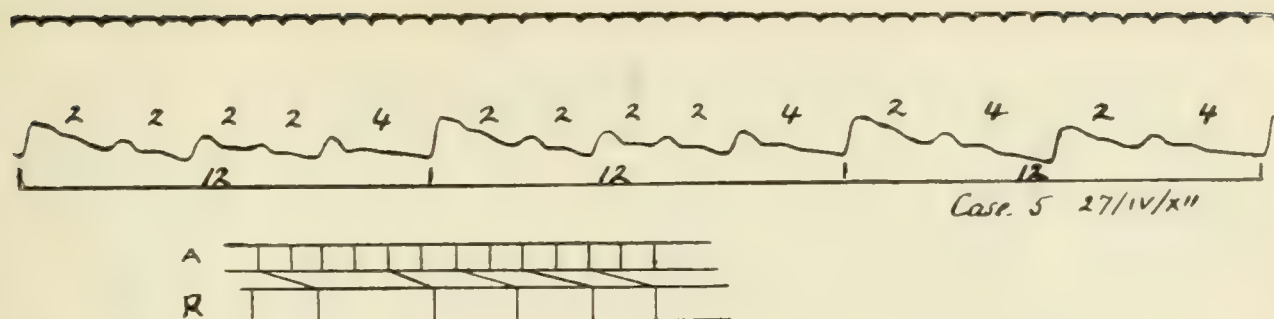


Fig. 7. An arterial curve from a case of flutter. The pulse is very irregular and bears a superficial resemblance to that of auricular fibrillation. Note the presence of alternation. An explanatory diagram, in which the relations of auricular contractions and radial upstrokes are illustrated approximately, accompanies this figure.

Fig. 4 shows the passage of a 4 : 1 period into a 2 : 1 period. Again the bracketed stretches are exactly equal; one corresponds to two 4 : 1 cycles, the other to four 2 : 1 cycles. It should be especially noticed that I have avoided the actual point of change in placing the brackets; and I have done so for the following reason. Bracketed stretches can be legitimately compared, only *when the points of each single bracket coincide with similar upstrokes*. That is to say, the beats at the points of a given bracket must be preceded by equal pauses; this is essential in all such measurements, otherwise the pulse beats in question will not have been equally delayed (bundle conduction and presphygmie interval will have been variable) and they cannot be taken as indices of the intervals which separate the corresponding auricular systoles. The first 2 : 1 cycle in Fig. 4 is longer than the rest; it is a strong beat and the auricular systole which was the cause of it took place at a shorter interval before it, than was the case with the succeeding beats. The last were all delayed in their appearance. Considering this first cycle of the faster rhythm, we have the choice of marking it as a 2 : 1 or a 3 : 1 cycle. Comparing it with the evident 2 : 1 cycles, it is shorter than  $1\frac{1}{2}$  of these and longer than one of them. That a 2 : 1 cycle in this position would be relatively long is to be anticipated for the reasons stated, that a 3 : 1 cycle in this position should be relatively short is opposed to experience. Consequently, in the analysis of the remaining curves, when a cycle is longer than the calculated duration of  $x$  number of auricular cycles, such a cycle is marked  $x$  or  $x + 1$  according to whether a long or a short cycle, respectively, precedes it. In adopting this system, I am merely following the well known rules of pulse analysis. That the rule is sound will be evident from a consideration of Fig. 2. Here I have marked the cycles according to this system where a stretch of a 2 : 1 ratio passes into an irregular stretch. If the cycles have been correctly marked, then the first seven cycles of 2 : 1 heart-block, which are bracketed, should be exactly equivalent to the next five cycles of the irregular period, which are also bracketed; for each bracketed stretch should correspond to fourteen auricular cycles. Such is actually found to be the case.

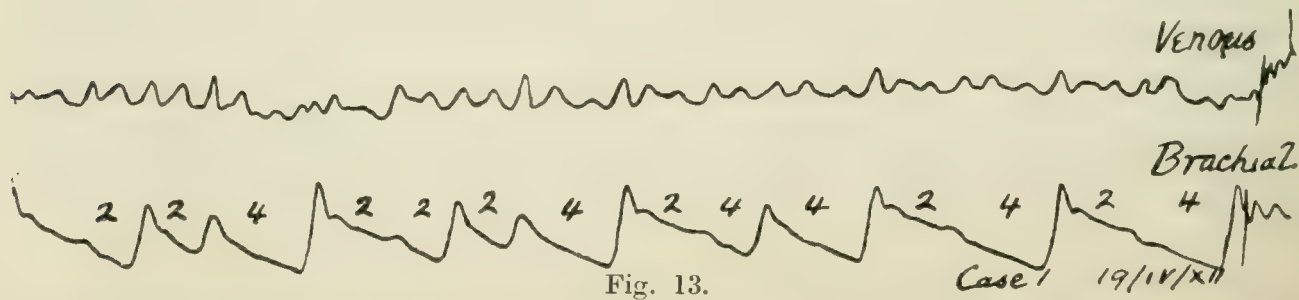
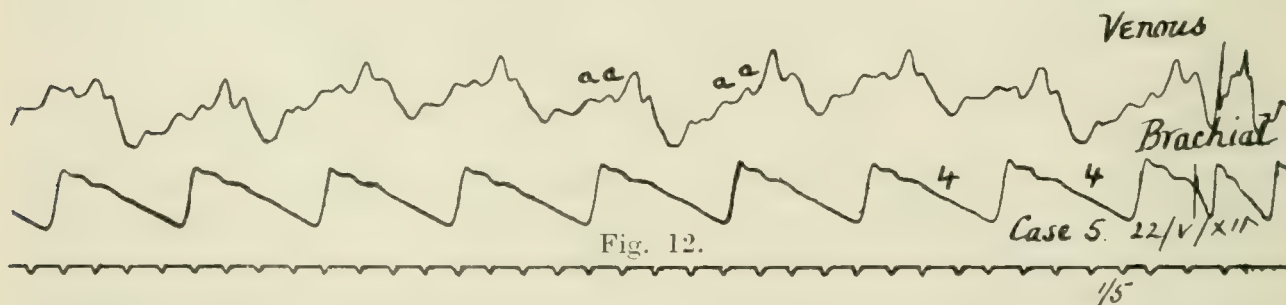
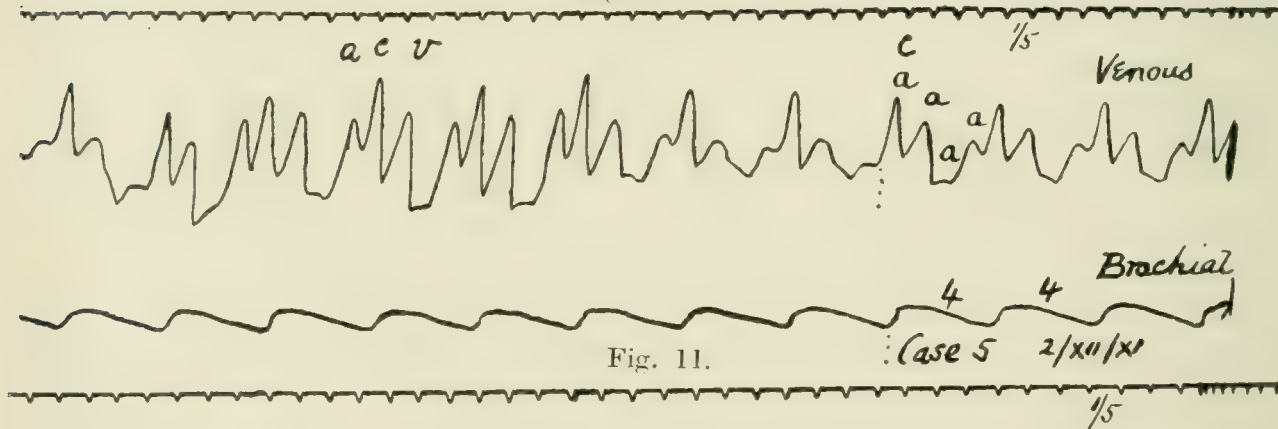
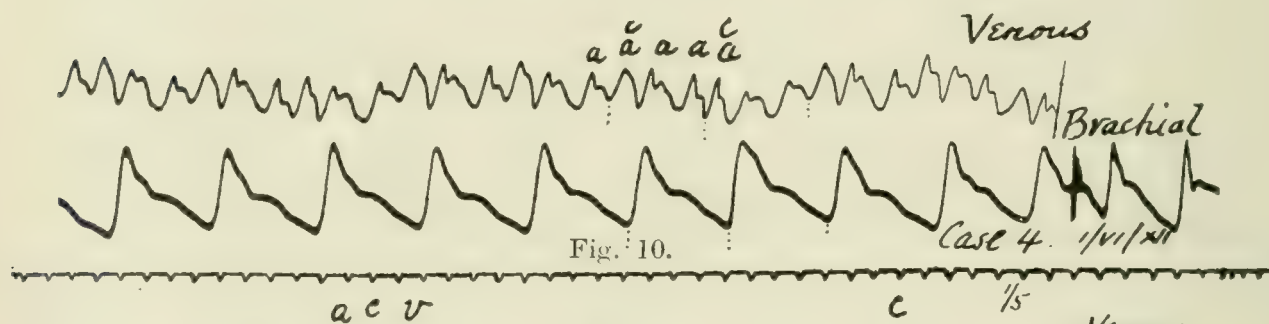
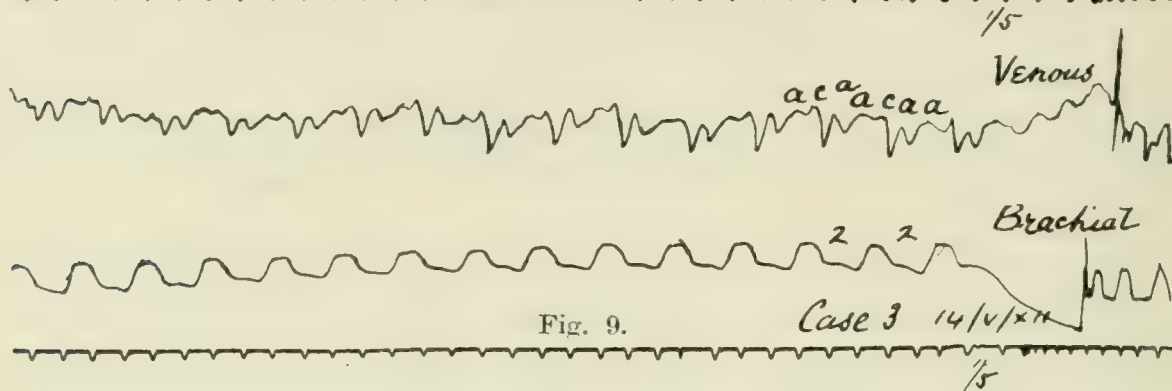
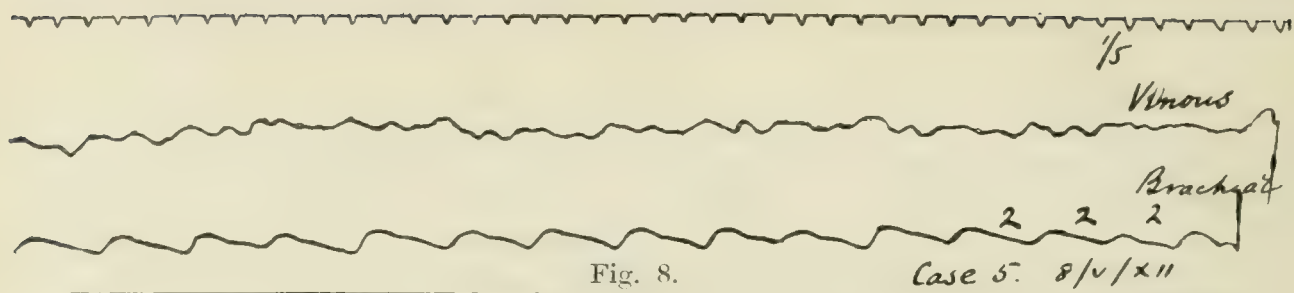


Fig. 8-13. Six polygraphic curves, showing the types of venous tracings which accompany auricular flutter.



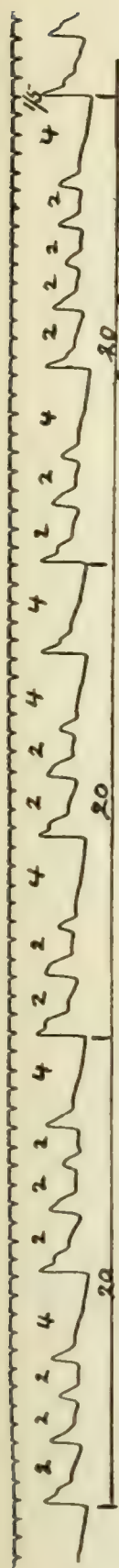


Fig. 14. An arterial curve from a case of flutter, showing an irregularity which superficially resembles that of auricular fibrillation.

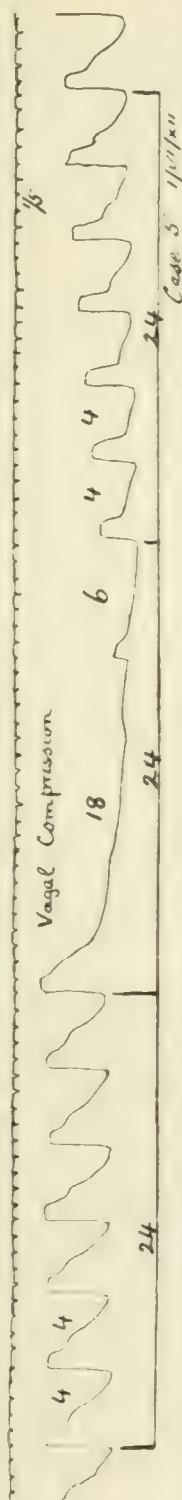


Fig. 15. An arterial curve showing the effect of right vagal compression during a period of 4:1 heart-block. The auricular rate is unaffected; the ventricular responses, after the long pauses, occur at expected intervals. Note the weakness of the returning pulse waves.

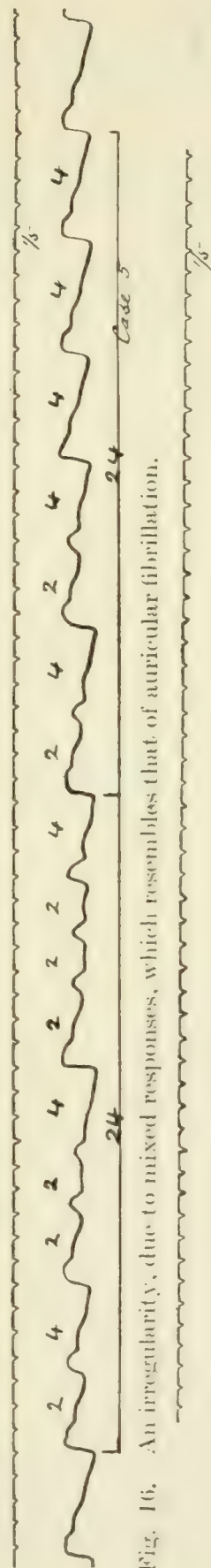


Fig. 16. An irregularity, due to mixed responses, which resembles that of auricular fibrillation.

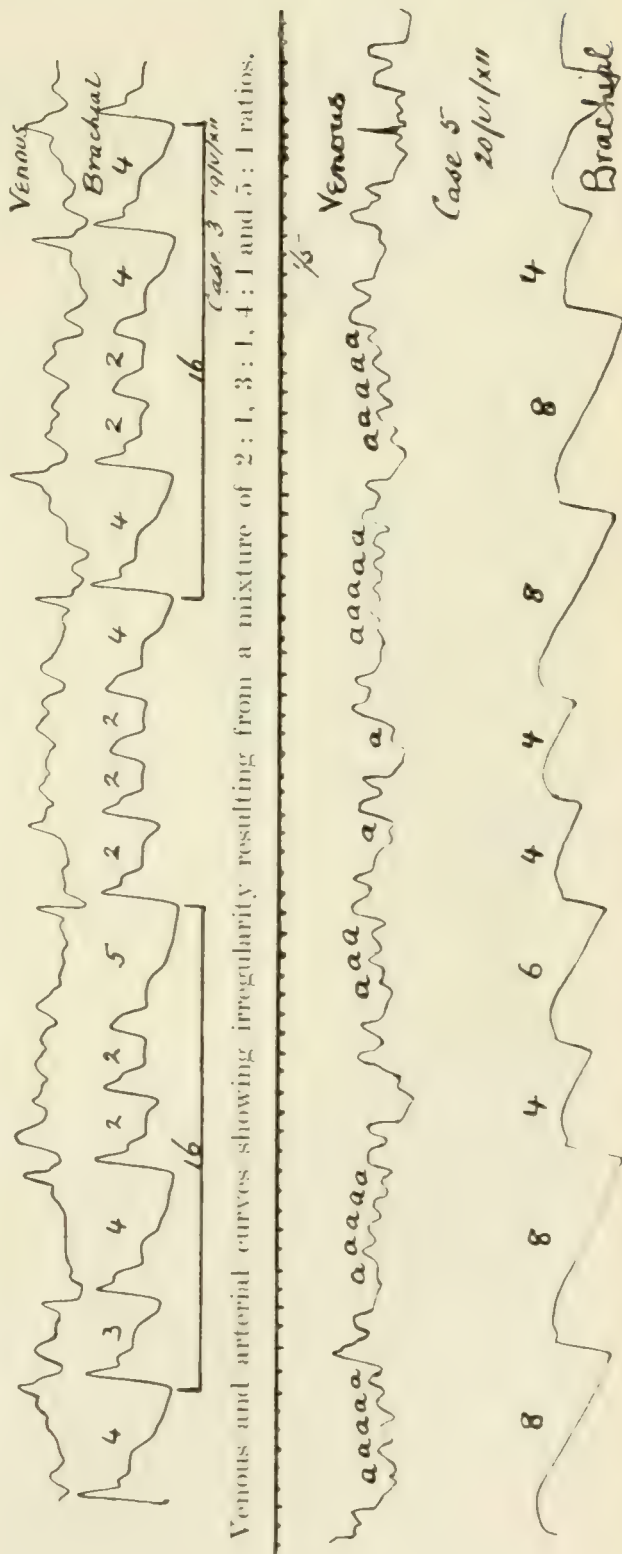


Fig. 17. Venous and arterial curves showing irregularity resulting from a mixture of 2; 1, 3; 1, 4; 1 and 5; 1 ratios.

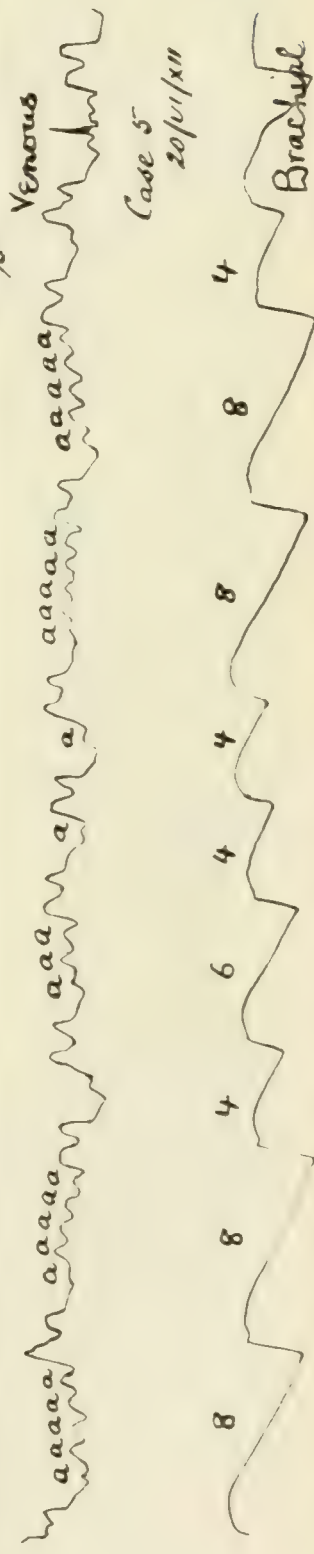


Fig. 18. Venous and arterial curves, showing irregularity as a result of a mixture of 4:1, 6:1 and 8:1 ratios.

Similar analyses are shown in Fig. 7, 13, 14 and 16, but in these figures the pictures are further complicated by the presence of conspicuous alternation; and in Fig. 13, certain of the beats are so weak that they barely affect the arterial curve; also the increased delay in certain beats of this figure is exceptional.

One of the chief reasons why the arterial curves accompanying auricular flutter should be thoroughly comprehended, is their possible confusion with the curves of auricular fibrillation. I have already indicated the manner in which they may be distinguished. The longer curves of Fig. 14, 16 and 17 illustrate this point especially. A cursory examination might easily lead to an erroneous conclusion. In Fig. 14, three equal stretches are bracketed. These are stretches of some length and the arrangement of the beats within them is variable. The pulse beats show groupings; batches of three and four occur. The curve may be split into shorter stretches. There are two groups of four beats which are equal in length, and there are three groups of three which are equal. Moreover the two groups of four beats are arranged in an exactly similar manner, as are also the three groups of three beats. This is a phenomenon which is never seen in auricular fibrillation, a fact which I have emphasised in my book.<sup>4</sup> In Fig. 16, two stretches, each corresponding to twenty-four auricular cycles, have been bracketed. The stretch to the right may be subdivided into two, each equivalent to twelve auricular cycles; there are also three stretches exactly equivalent to six auricular cycles; three exactly equivalent to eight; and three exactly equivalent to ten, in this single curve.

In Fig. 18, similar analysis shows the presence of mixed 4 : 1, 6 : 1 and 8 : 1 periods; an analysis which is substantiated by the corresponding venous tracing.

So far I have dealt with the analysis of periods in which the ratio of auricular to ventricular contraction is as 2 : 1 or as simple multiples, *i.e.* 4 : 1, 6 : 1 and 8 : 1. In such curves, and in the absence of electrocardiograms, the full analysis is impossible, for the periods might be interpreted with perhaps almost equal justification as 1 : 1 periods, and the simple multiples, *i.e.* 2 : 1, 3 : 1 and 4 : 1, on the assumption that the auricular rates are 120-150 and not 240-300. We now come to the less frequent arterial curves, which by themselves disclose the true auricular rate. They are curves in which cycles occur which are exactly intermediate between certain of those already considered. If our choice lies between the interpretation of a mechanism as consisting chiefly of :—

2 : 1 and 4 : 1 periods or

1 : 1 and 2 : 1 periods,

then the appearance of a cycle of intermediate length may be of great value. Fig. 1 shows the interruption of 2 : 1 heart-block by an exceptionally long interval. It is almost exactly equal to two cycles of the faster rhythm; but it is not a 4 : 1 period; were that the case its length would be less, for



the large beat which succeeds it should have a short *As-Vs* interval. It is in reality a 5 : 1 period ; it is longer than the 4 : 1 periods of Fig. 14, which is from the same case. This analysis is completely justified by measurement of a stretch of curve taking in the whole disturbance. I have marked two equal stretches of curve ; the first contains six cycles of equal length ; the last contains one long cycle, and three and a half shorter cycles. If we adopt a simple analysis, and call the shorter cycles 1 : 1 periods, it is necessary to assume that, over the period of irregularity, the auricular rhythm has been disturbed, and disturbed in a peculiar manner ; somewhere an auricular cycle has been curtailed by exactly one half. The possibility of such a coincidence cannot be allowed. On the other hand, the whole curve is fully explained if we assume the higher ratio. In a series of auricular beats which might be labelled successively *a* and *b*, the responses before the disturbance are to *a*, the responses after the disturbance are to *b*. A parallel example is shown in Fig. 6.

From time to time, it happens that two of these *odd* ratios lie close together so that two may be taken into a single bracketed stretch. Fig. 17 is an example of this kind. Two stretches are bracketed in this figure ; each corresponds to sixteen auricular cycles. The second stretch is built up of *even* ratios, represented by 2 : 1 and 4 : 1 periods. The first stretch is built up of 2 : 1 and 4 : 1 ratios and, in addition, two *odd* ratios, represented by a 3 : 1 and 5 : 1 period, are interposed.

Thus it is evident that from time to time, where no 1 : 1 periods occur, full knowledge of the auricular rate may be obtained from a detailed analysis of arterial curves alone.

### *The venous curves.*

The venous curves, when the auricles contract at extreme rates, are very varied in form, and the variability mainly results from the different degrees of heart-block which may be present. Where the heart-block is of high grade, be it complete or partial, as in Hertz and Goodhart's case or in Jolly and Ritchie's patient, and the ventricular rate is slow, the auricular waves may be distinct or even prominent.\* When the ventricular action is fast, the auricular waves are usually indistinct or almost absent.

It is necessary that the forms of venous curves which accompany auricular flutter should be borne in mind, for not only are these curves often but imperfect guides to the identification of the condition, but they may actually mislead. This is especially so when patients first come under observation, for at such times the ventricular action is usually rapid. The auricular beats are close together, and the period of auricular diastole is of the shortest ; the ventricular systoles are also close set ; consequently, when a 2 : 1 ratio

---

\* As a general rule too the auricular waves are more prominent as the rate of contraction is lower.

is present, each auricular contraction falls partly within the period of ventricular systole. In all probability there is considerable engorgement of the auricle as a result ; the weakness of its systole is thus readily accounted for. Whatever the explanation, the fact remains that when a regular 2 : 1 ratio is present, the venous curve usually consists simply of rapid and small undulations in which it is difficult, nay often impossible, to identify the expected waves with certainty. Examples of curves of this nature are seen in Fig. 5, 6, 8 and 9. When a regular 4 : 1 ratio is present, the *a* waves may be clear only towards the ends of the diastolic periods, as in Fig. 12. In rare instances of 4 : 1 or even a smaller ratio (*i.e.* 3 : 1 or 2 : 1) they may be distinct throughout (see Fig. 10 and the curves of Turnbull's and Rihl's cases). Sometimes the phlebograms are of such a form that they are readily misinterpreted ; in Fig. 11, I have marked what would appear as the obvious interpretation to the left (*a*, *c* and *v*) ; electrocardiograms taken on the same day demonstrated the correctness of the second interpretation, which is seen to the right of the figure ; the curve was taken while 4 : 1 heart-block was present. When long pauses occur between ventricular beats, signs of the auricular beats are sure to occur from time to time, as in Fig. 5 and 6 ; usually they are more evident than these figures suggest ; thus in Fig. 18, they are perfectly clear, and especially so towards the ends of diastoles. Each venous wave in Fig. 18 may be taken to represent an auricular contraction ; the least distinct is that which falls at the commencement of diastole.

#### *General features of the electrocardiograms.*

The electrocardiograms have been described already in illustrating the mechanisms presented by the separate patients of the series. It remains only to note certain features which are almost common to the curves of flutter and briefly to discuss these features.

The portions of the electrocardiograms which represent the auricular activity are peculiar in more respects than one. If we except the curves shown in Fig. 33, where the auricular rate is relatively slow, the auricular complexes in leads *II* and *III* are always contiguous ; that is to say, the separate electric complexes are so close together that the end of one marks the beginning of the next. The string is in constant motion ; there are no isoelectric stretches dividing one auricular electric cycle from the next. That the whole electric cycle corresponds to auricular systole is not possible, for if that were the case diastole would not be represented. It might be argued that diastole is so short that the isoelectric line, which we expect, is inappreciable and escapes observation. But this possibility may be excluded. The normal length of *P* is decidedly less than .20 sec. ; and if the auricular rate is fast *P* is shorter than this. If we measure the length of an auricular cycle in Fig. 31 we find it of approximately .22 sec. duration, despite the extreme rate of auricular contraction shown by the figure. The length of an



auricular electric cycle in flutter is inversely and exactly proportional to the rate. Thus, if the rates are 300 and 270, then the lengths of the individual cycles are  $\frac{60}{300}$  and  $\frac{60}{270}$ . It follows that during auricular diastole electric potential is developed in the auricle. This observation is not an isolated one. The same fact has been noticed for the ventricle, when its movements are extremely rapid (see Levy and Lewis<sup>3</sup>). That potentials are developed in diastole has also been shown for a slowly beating ventricle. The *U* wave, originally described by Einthoven, lies in diastole.<sup>6</sup> Although the electric curves may indicate the onset of auricular systole in flutter, they are but imperfect guides to the onset of diastole. It seems probable that, both in the case of the auricle and of the ventricle, chemical processes which occur in diastole are responsible for the string deflections. And as these diastolic deflections are always related to the commencement of diastoles, it seems natural to ascribe them to the more rapid reparatory metabolism which may be assumed to attend these phases of the cardiac cycles.

The auricular complexes in auricular flutter are remarkable for their constancy of form from case to case. Except again Fig. 33, and so far as curves have been published, the following statements are universally applicable. *P* in lead *I* is either a small and pointed summit, or is so insignificant that it cannot be found. *P* in lead *II* and *III* runs on either side into the adjacent complexes, so that a series of such complexes form a continuous wavy or zig-zag line; the auricular complex is found to be almost if not quite a purely convex summit wherever its onset can be defined.

The resemblance in shape and amplitude between auricular cycles from case to case is often so close that it suggests a distinct and special auricular mechanism. I draw particular attention to the forms of the complexes in Fig. 20, 29, 31, 32, 34 and 35, each figure being from a separate case. In all these the outlines are practically identical. There is a relatively abrupt upstroke and a relatively more inclined downstroke. The curves of *CASE* 8 are so similar to those of this series that it is unnecessary to publish them. The published curves of *CASES* 10, 11 and 14 were of the same form. Speaking of the curves of 13 cases in which electrocardiograms have been obtained, they conform to this type in no less than ten instances. If we compare the complexes in Fig. 28 and 29, it will be seen that the usual type is more distinctly assumed when the heart-block is of higher grade. Of the three remaining cases out of the thirteen, one (*CASE* 5) showed the usual type of complex during 4:1 heart-block stage; thus leaving two real exceptions (*CASES* 1 and 6 of the present series). In one of these (*CASE* 6) the auricular rate was relatively slow; in the other (*CASE* 2, Fig. 24) the divergence of type is not great.

It seems probable to me that this resemblance may largely result from the extreme auricular activity. The contiguity of separate auricular cycles is certainly to be assigned to this cause; if the further resemblances arise in similar fashion, then it should be capable of experimental proof. It is at least remarkable that in the single case where no resemblance can be traced

(Fig. 33) the auricular rate is decidedly less than in the remainder, namely 228. In *CASE 5*, the lowest auricular rate recorded electrocardiographically was 256, and of the curves for this day it may almost be said that contiguity is broken. It seems, therefore, that if contiguity is the result of great acceleration, such contiguity is fully established when the rate reaches 260 or surpasses it.

*The acceleration of the auricles.*

The lowest rate of auricular contraction in the series of collected cases was 200, the highest rate 330. A number of the cases have developed rates equal to or exceeding 300 (*CASES 1, 3, 5, 6, 10, 11, 14 and 15*). A notable quality of these accelerations is their relative constancy under different conditions. In *CASE 1*, the rate varied between 312 and 324; in *CASE 2*, between 266 and 289; in *CASE 3*, between 264 and 324; in *CASE 4*, between 260 and 278; in *CASE 5*, from 244 to 300. And these counts are of rates found over long periods of time and under very varying circumstances. From day to day the correspondence of rate is often remarkable (see especially *CASES 4, 3 and 5*). The changes of rate with posture are almost negligible; in *CASES 2 and 3* pulse counts were taken and no differences were noted. In *CASES 4 and 5* counts were made from pulse curves; the ventricular rate was less than three beats faster per minute in the standing position in one case, and no constant differences could be found in the other.\*

In two of my patients, electrocardiographic records were often taken shortly after they came to the school; they walked some distance; other records were taken after they had rested. In none of the records taken on any one day can an appreciable change in auricular rate be found. In two patients (*CASES 4 and 5*) continuous records of the pulse (during periods of 2:1 ratio) were taken, commencing directly after exercise; little or no change of rate could be detected. In three patients in which counts could be made, pressure upon the vagus, sufficiently strong to stop the ventricle for periods of several seconds, had absolutely no effect on the auricular rate. Rihl noticed the same fact. The fast rhythm appears to be almost uninfluenced by conditions which materially change the rate of the normal pulse. I have repeatedly noted the same stability of rate in cases of paroxysmal tachycardia of lower grade, and have spoken of it in previous papers. Rihl has also been impressed by it in flutter, and has concluded from this observation that the acceleration is due to over-action of the sympathetic, while the vagus influence is entirely in abeyance. But this view is one which, it seems to me, has insufficient facts to support it; and my belief is dictated by the following arguments.

---

\* In all cases the observations were made during periods of 2:1 ratios.



It is necessary to bear in mind that we are dealing with a heart action which is very probably ectopic in nature; it may not be derived from the normal pacemaker.\* The reason for regarding the rhythms as ectopic is that the auricular complexes of the flutter period differ so essentially from those of the normal period; the comparison can be made in the curves of my first article (*CASE 5*). It may also be made in the curves of *CASES 1, 2, 14, 15 and 16*. When my first article was written, I was more definitely of opinion that the new rhythms of flutter are ectopic, and for the reason which influenced Rihl. The auricular complexes were read as inverted complexes. Further examination of a more extended series of curves shows that this is almost certainly not the case. The divergence from the normal is therefore actually less than it was considered to be; nevertheless it is considerable. Whether it can be ascribed wholly to change of rate remains to be proved; but I think that change of rate is not the sole reason, after comparing the complexes of the flutter and of premature beats in the same case (*CASE 5*); the latter are undoubtedly ectopic and are not dissimilar to the complexes of the flutter.

So long as we are in doubt, the possibility that the rhythms are ectopic remains and should be taken into account, and this more especially because, if ectopic, the special nerve relations can be explained. Tachycardias of lesser rate show the same failure of reaction to nerve influences, as I have pointed out. If one class (flutter) is to be explained by overaction of the sympathetics, so also must the other, if Rihl's arguments are permitted. These slower tachycardias can often be demonstrated beyond doubt to be ectopic. In the slower tachycardias of auricular origin the absence of nervous control may be ascribed to the altered anatomical relation between nerves and pacemaker. We are not justified in assuming anything in regard to the innervation of new centres of impulse formation until more experimental facts have been obtained. I am aware that in certain experiments, notably those of Rothberger and Winterberg, in which the auricles were under the influence of poisons ( $\text{BaCl}_2$ , &c.) sympathetic stimulation led, not only to a dislocation of rhythm, but also to acceleration of it. It remains to be shown that the conditions are comparable to those now studied. At all events, because the heart rate is greatly accelerated it does not follow that the sympathetic nerves are in any way to blame. Extreme accelerations of the ventricle may be induced by ligation of a coronary artery or a small branch of such a vessel; and such tachycardias are evidently the result of nutritional disturbances of intracardiac origin; they have nothing to do with the extrinsic cardiac nerves. It may be that in many instances of tachycardia the nerves of the heart ultimately provoke the new rhythm; such a statement cannot be denied; neither in the present state of our knowledge can it be justly affirmed. We know that in the normal heart, new and rapid rhythms cannot be provoked by such stimulation. It is

---

\* Rihl recognised this possibility, but his reasons for a conclusion to this effect are not convincing, neither, if it be true, does he appreciate its full significance.

necessary that the organ should be brought first into a curiously sensitive condition, whether by the injection of adrenalin, the chlorides of barium or calcium or by chloroform or perhaps by simultaneous vagal stimulation, before sympathetic excitation is successful. The question is an important one, for so long as we accept the view, adopted as I think prematurely by Rihl, so long shall we look for the cause of the whole disturbances in the central nervous system; whereas it seems to me, our first endeavour should be the exclusion, at all events, of a primary cardiac defect. There are clear connecting links between these extreme accelerations and premature contractions and slower tachycardias on the one hand, and fibrillation of the auricles on the other. These disturbances are associated in most instances with distinct evidences of cardiac lesions; and there is every reason to believe that the extreme accelerations with which we are now dealing are of similar origin. All appear to be part and parcel of the same process, namely, heterogenetic\* impulse formation in the heart. It is clear that such impulse formation can result apart from all nerve influences (*i.e.*, in obstruction of an artery); it is by no means so clear that it can result from morbid nerve influences playing upon a perfectly healthy organ.

*The response of the ventricle.*

Patients in whom there is an auricular action exceeding 200 per minute usually present a slower ventricular rate, as illustrated by the present series of cases. Of the sixteen cases in which graphic records of auricular flutter have been obtained, all have shown heart-block from time to time and it has been either constant or present on most occasions; the lowest grade of block has usually been a 2:1 ratio, or response of the ventricle to each second auricular impulse. It is in this condition that the patients usually come under observation for the first time. That lower rates may occur while no drugs are being administered will be evident from Jolly and Ritchie's report (CASE 10), in which complete-heart block was present both before and after the onset of the flutter; and also, though less clearly, from Hertz and Goodhart's case,<sup>14</sup> for here the responses were at wide intervals; but this case was complicated by the presence of premature ventricular contractions. When the ventricle is beating at half the rate of the auricle, and the latter contracts 300 times in the minute, it may be asked whether the tissues joining auricle and ventricle are functionally defective? This question appears to be answered by the occasional occurrence of a 1:1 response in the same cases; rates of 290 and 300 were reached by the ventricle and were recorded by Mackenzie (CASE 14), and it is more than probable that 1:1 response occurred from time to time in CASE 6. It may be concluded that the junctional tissues can conduct impulses which succeed each other at this rate and that the ventricle can respond to them. When 2:1 heart-block is seen, it may be said therefore that there is a primary

---

\* This term has been fully described in my book "The Mechanism of the Heart Beat."



deficiency of conduction, but this deficiency is probably slight, for acceleration of the auricle tends to exaggerate the degree of heart-block, as has been clearly shown experimentally.

While discussing the electrocardiograms, it was pointed out that the auricular representatives are as a rule convex. The *P* summits, which are contiguous, commence in upstrokes, a fact which was deduced from their form in lead *I*. If we measure the length of the *P-R* interval in this lead in Fig. 28, it is found that it amounts at the most to .1 sec.. Considering that 2 : 1 heart-block is present, this interval is much shorter than might have been anticipated ; and its brevity suggests that the ventricle responds to the preceding auricular contraction. That such is the case is demonstrated, I think, from an examination of electrocardiograms which show irregular ventricular action in the same case. Fig. 36 exhibits a single 5 : 1 period which is followed by successive 2 : 1 periods. Consider the upstrokes of *P* which precede the second and third *R* summits in this photograph. The first lies further from the corresponding *R* summit than does the second. If the two ventricular beats in question were each responses to the preceding auricular summits, then the *As-Vs* interval of the first cycle would be the greater ; but this *As-Vs* interval follows the longer instead of the shorter pause. We know from the arterial curves that the *As-Vs* interval is varying in the ordinary manner during periods of irregularity ; that is to say that the shorter pauses are succeeded by the longer *As-Vs* intervals. It must be also the case in this figure. If the first ventricular beat is a response to the preceding auricular contraction, then the second is a response, not to its preceding auricular contraction, but to that which is further removed from it. Such is the interpretation which has been marked upon the figure. The remaining cycles of the figure are all of 2 : 1 ratio, and as the *Vs-Vs* interval shortens gradually for the first few beats, so the *As-Vs* interval is seen to increase slightly. As a result the auricular contraction which gives rise to a ventricular response is eventually placed so that its upstroke coincides with the commencement of the preceding *R* summit. In this figure the reason why the first cycle of a 2 : 1 period is relatively long is clearly seen ; its unusual length depends upon the arrangement of *As-Vs* intervals. The figure is also of interest because it shows alternation, which commences with the third of the rapid arterial upstrokes. It does not commence with the second, as is usual, for the reason that a longer pause precedes this beat.

Another example of simultaneous arterial and electrocardiographic curves is shown in Fig. 37. This was taken from another case (CASE 5), and the ratios for the separate cycles are clear. A bigeminal action, consisting of 2 : 1 and 4 : 1 periods passes into a simple 2 : 1 heart-block. The figure illustrates to perfection the impossibility of accepting the interval between adjacent *P* and *R* summits. It is known from the electrocardiograms given by lead *I* in this case (for examples, see previous article), that the upstrokes represent the commencements of auricular systoles.

If we take those upstrokes in Fig. 37 which directly precede *R* summits, the *As-V*'s interval decreases after the longest pauses to less than .07 secs.,\* and the greater part of the auricular systole is buried in the ventricular systole. The responses must therefore have been to auricular systoles which were further removed, as illustrated by the diagram drawn on the figure. Thus it seems clear that in pure 2:1 curves, the responses are as marked upon Fig. 28; it is also evident that two auricular systoles may occur, and that before the first of them is responded to by the ventricle, the second auricular systole may be almost completed; it is also obvious that two auricular impulses may be travelling along the junctional tissues at the same moment.

The deficiency, when a 2:1 ratio is present, is attributable to pathological change rather than to auricular acceleration pure and simple; the hearts in which flutter occurs are abnormal. The demonstration of imperfect conductivity, which occurs so constantly in these cases, is of considerable importance. Clinically and pathologically the cases are closely allied to those which exhibit auricular fibrillation, and they warn us most clearly against the conclusion that in auricular fibrillation all the impulses are transmitted. Later we shall see that there is good reason for believing that the contrary conclusion is more justifiable.

Cases of auricular flutter are of importance because they permit exact observations upon changes in conduction in the human heart. One factor is practically constant, and so far as we know it is constant in no other condition,† the auricular impulse rate is unvarying. Constancy of the auricular impulse rate is important because, as I have stated, variations in auricular rate in themselves alter conduction. Observations upon heart-block, where the normal rhythm is present, are not pure, because this factor has always to be taken into consideration. In all the cases which have come under my observation, nothing has been more fully established than that exercise and excitement immediately increase the rate of the ventricle, the rate of the auricle remaining practically unaltered. I have made a great many observations from this point of view. In *CASES* 3, 4 and 5, rising from the lying to the sitting or standing posture would almost invariably and immediately change a 4:1, or irregular response, to the original 2:1 response. In *CASE* 3, this effect was most conspicuous. While this patient was upon digitalis or strophanthus he often walked as far as the school. When he arrived, the ventricular contractions were always regular and at a half the auricular rate. If he lay for a few minutes the pulse became irregular and slower, and mixed responses (2:1, 3:1, 4:1 and 5:1) were then observed. Often he sat with his arms and foot lying on the electrodes preparatory to the taking of curves, and the regular and fast ventricular rate would be

---

\* A time-marker is not shown in this figure but the auricular rate was calculated on the same day in other curves to be 272 per minute. The *P* summits are separated therefore by intervals of .22 secs..

† It is possibly constant in auricular fibrillation.



maintained ; on many occasions if he raised the right foot and rested it upon a chair a slower and irregular action immediately appeared. And it would disappear and reappear with great constancy according as the leg was in the more strained position, while sitting, or horizontal. The reaction was an extremely sensitive one. If I wished to obtain arterial curves of the irregular periods, it was usually insufficient to strap the receiver to the outstretched arm, the arm required support before the pulse became slow. The tension in the upraised arm was almost always sufficient to establish temporarily the fast and regular action of alternate responses. A few minutes conversation, or an unexpected visit, always provoked a higher ventricular rate. The rate was almost always faster after meals ; swallowing never seemed to affect it in this or the other patients. When the patient lay quiescent and the heart beat irregularly, breaking from regular 2 : 1 periods into irregular periods of higher ratios, the reason for the individual changes could not be ascertained. Breathing had no relation to them.

In all those cases of this series in which digitalis or strophanthus was administered, the original grade of heart-block was increased. Hearts in which the auricles are in a state of flutter appear to be peculiarly susceptible, as are those in which the auricles are fibrillating, to the action of drugs of this group. This susceptibility is largely attributed to the rapidity with which impulses are showered upon the junctional tissues. A condition of 2 : 1 block is rapidly converted to one in which there are mixed periods of 2 : 1 and 4 : 1, or 2 : 1, 3 : 1, 4 : 1 and 5 : 1. Eventually in most cases 4 : 1 heart-block is established. The block may increase further in some instances (see *CASE 5*) and 6 : 1 and 8 : 1 periods may be observed. Personally I have not employed atropine, but Rihl has used it on several occasions in one patient ; where digitalis heart-block is present atropine restores the original ventricular rate, according to this writer. It appears therefore that the action of digitalis in this instance was chiefly if not entirely an indirect one through the vagi.

Rihl found that pressure on the carotid sheaths produced slowing of the ventricle (an increase of block) in his cases. The same observations have been made repeatedly in three cases of my own series (*CASES 3, 4 and 5*). In each instance pressure upon the carotid sheath increased the grade of block ; the vagi appeared to be particularly sensitive to even light pressure and in one case (*CASE 5*) the application of the jugular receiver to the neck on certain days was almost always followed by slowing of the ventricle. It was a matter of indifference as to which side was pressed upon ; the effect was equally conspicuous upon the left as upon the right side. In the three cases in which I have tested the effect of vagal pressure, the procedure gave a positive result more readily when the patient was under the influence of digitalis or strophanthus. Control observations were made in two cases (*CASES 4 and 5*) ; in one (*CASE 5*) patient I could obtain no effect at all even with the deepest pressure while the patient was uninfluenced by drugs ; in the other 2 : 1 heart-block was temporarily converted to irregular responses

at 3 : 1, 4 : 1 and 5 : 1 intervals. It is not evident from Rihl's paper whether his patients were under drug influence when the observations were made, except in one instance when the patient was upon digitalis. There was no demonstrable effect upon the auricular rate on any occasion ; the result was always a pure conduction effect. These results are of importance because they suggest the control of the junctional tissues by both vagal nerves in the human subject ; and because they fail to substantiate a view that there is a preponderating influence of one nerve over the other. Examples of the curves obtained are shown in Fig. 15 and in an electrocardiogram of my previous article.

A study of the reaction of the ventricle to the rapidly beating auricle reveals an interesting relation between the rates in the two chambers. There is a remarkable tendency for the ventricle to respond so that the ratio is an even one. 2 : 1 heart-block is the commonest relation of any, the only other ratio which at all commonly gives rise to a regular ventricular action is a 4 : 1 ratio. On one occasion and on one only, the ventricle has beaten in response to each third auricular stimulus, and then only for short spaces of time. When the ventricle is irregular, the irregularity usually consists of mixed 2 : 1 and 4 : 1 periods. Sometimes, it is true, isolated 3 : 1 and 5 : 1 periods appear ; but they are rare by comparison. In the single instance in which a higher grade than 4 : 1 heart-block was seen (CASE 5) the longer pauses consisted of 6 : 1 and 8 : 1 periods. Even ratios are far too common to be accounted for by coincidence, though it must be acknowledged that an explanation of the phenomenon is difficult. The fact remains that when the ventricle is slowing in these cases, so as ultimately to beat at a fourth of the auricular rate rather than a half, it tends to pass into a condition in which 2 : 1 and 4 : 1 periods are mixed and not to exhibit regular 3 : 1 ratios. Samojloff has drawn attention to the similar method of response of the frog's heart, in which conduction disturbances have been induced experimentally.

*The relation of auricular flutter to other morbid auricular mechanisms.*

In an article written in conjunction with Dr. Schleiter, I have already drawn attention to the close relation between paroxysmal tachycardia of auricular origin and auricular fibrillation. The conclusion that they are part and parcel of the same pathological process was supported by a number of facts, none of which were more noteworthy than the frequent occurrence of the two conditions in the same patient, and especially the immediate passage of one to the other. The argument applies even more strongly to auricular flutter, for in thirteen cases of the present series auricular fibrillation occurred in seven, and in six, one condition passed directly into the other.\* The separate mechanisms must be very closely related ; and it is probable

---

\* The actual transition was seen in one case only (CASE 14), and in this one a number of such transitions were recorded.



that they have a similar pathogeny. The occasional occurrence of tachycardia of a more simple form (*CASE 2*), and the frequent occurrence of single premature beats in the same patients when a sinus rhythm has been re-established (they were present in five out of the six cases in which the normal mechanism was observed) seems to connect flutter with the remaining auricular mechanism in which disturbing beats are found.

The conclusions that

1. Single premature auricular contractions,
2. Small groups of the same,
3. Paroxysms of tachycardia from single auricular foci,
4. Auricular flutter,
5. Paroxysms of tachycardia from two or more auricular foci, and
6. Auricular fibrillation

arise essentially in the same manner, namely, through the pathological or heterogenetic origin of new impulses in the auricle, are clearly suggested by the facts at our disposal.

*The number of impulses which reach the junctional tissues in auricular fibrillation.*

The passage of regular tachycardia of auricular origin into auricular fibrillation permits a theoretical comparison of the number of impulses which reach the junctional tissues in the two conditions. It is known from experiment that an acceleration of the auricles in the presence of a slight grade of heart-block tends to reduce the ventricular rate, and that the greater the auricular acceleration, the slower is the action of the ventricle. In the past we have had no data which have permitted us to gauge the rate at which impulses reach the junctional tissues when the auricles fibrillate. The view that all pass in experiment is but pure assumption. It may be that each second or each third impulse is transmitted, or that they are carried irregularly. That all pass in clinical cases is certainly not the case, for while in experiment the rates of the ventricular responses are always high, in patients they are variable and may be very low. We may argue that if the heart-block is present and the auricular flutter passes into fibrillation and the rate of the ventricle is reduced, the impulses are more frequent in the last named condition. We may make this comparison of rates in several cases of the series. In *CASE 1* the rates of auricle and ventricle before fibrillation appeared were 324 and 81, respectively. At the onset of fibrillation the ventricular rate was 79. In *CASE 2*, the auricular rate varied between 266 and 333; at the onset of fibrillation the pulse rate fell from 70-96 to 48-68. In *CASE 5* the auricular rate was 288-300, and at the

onset of fibrillation the pulse rate fell from 72 to 44. In Mackenzie's case (CASE 14) the auricular rate was 280-300 and at the onset of fibrillation the pulse rate fell from 140 to 55. Thus the ventricular rate becomes slower when fibrillation commences, or exceptionally, remains the same. It may be said of course that the heart-block resulting from digitalis has increased; but this seems improbable, for in most cases the degree of heart-block has been practically stationary for several days upon fixed doses of the drug. So far as these observations can be taken as evidence, therefore, it appears that the rate at which impulses reach the junctional tissues is greater while the auricles fibrillate than when they are in a state of flutter. The transitions suggest that a large proportion of the fibrillation impulses are always blocked in man even when ventricular rates of 200 are reached, and that the actual number of such impulses surpasses 270 or 300 per minute.

*Digitalis as a therapeutic measure in auricular flutter.*

In a previous article I recorded the passage of flutter to fibrillation during digitalis administration. A similar reaction was recorded in cases which, as it now appears, were of the same nature by Mackenzie and Turnbull. In the present paper I have added two further instances. In my original case the normal rhythm was resumed shortly after digitalis was withdrawn. The same phenomenon was witnessed in two cases which are now recorded (CASES 1 and 2). The normal rhythm was also resumed in Mackenzie's case and Turnbull's patient. It appears consequently that the production of fibrillation by digitalis administration is an important therapeutic measure in cases of flutter. The flutter may have lasted as long as four or five months (CASES 2 and 15); in fact, it is usually a persistent condition; it may last for three years or more; fibrillation has abolished it for observed periods, varying from a few weeks to several years. The induced fibrillation is a temporary event, and at its offset it is not the original tachycardia but the normal rhythm which is restored. From these facts it seems likely that whatever the final cause of the flutter, it is not a persistent one and that its continuation for long periods results from a perverse habit which the auricles acquire. Fibrillation seems to act by submerging the original fast rhythm. During the course of experiments on animals, regular tachycardias which are induced by stimulating some portion of the heart wall sometimes persist; they may be abolished by inducing a tachycardia of a faster rate by stimulating another point; and when this second stimulation ceases, the normal rhythm is restored. The induction of fibrillation is equally effective in these circumstances. Fibrillation presumably acts in a similar fashion in clinical auricular flutter, and this is a view which may be held to support the conclusion that the impulses arising in fibrillation and reaching any single point of the auricular tissues (such as the point at which flutter originates or the outlet to the ventricle) are more numerous than those of flutter itself. The hearts which manifest



flutter of the auricle are especially susceptible to digitalis and strophanthus in another way. As has been recounted, the grade of block is almost always increased in the earlier stages. If the full reaction and the return to the normal rhythm cannot be achieved, at all events the ventricular rate may be reduced and the heart obtains rest.

*Summary and conclusions.*

1. A condition is described and is spoken of as “auricular flutter.” It is not uncommon clinically (sixteen cases are collected), and it occurs for the most part in elderly subjects. It is characterised by an extremely rapid auricular action; the rate being from 200 to 330 per minute (usually at about 300 per minute). Generally, when it develops, it persists for months or years; it may occur in shorter paroxysms.

2. The auricular rhythm is the result of pathological or heterogenetic impulse formation. The new rhythm is probably also ectopic. It is not under nerve control. The rate is wonderfully constant in most subjects and is practically uninfluenced by posture, exercise or nerve stimulation. Its persistence is probably attributable to habit rather than to a continuation of the exciting cause.

3. As a rule the ventricular rate is one half the auricular, but it may be the same as the auricular, or any grade of heart-block may be present. Thus the ventricle may beat at rates varying from 30 to 300; it may beat regularly or irregularly. The rate of the ventricle is controlled by the functional condition of the junctional tissues; conduction is decreased by digitalis and its allies, and increased by exercise. The heart-block is increased by vagal compression, and this seems to be especially the case while it is influenced by digitalis.

4. When 2:1 heart-block is present the *As-Vs* interval may be so long that the auricular summit *P* of one cycle may fall with the *R* summit of the preceding cycle. Two auricular impulses may be travelling towards the ventricle at the same time; the ventricle may not respond to an auricular impulse until the next auricular systole is almost completed. The ratio of auricular and ventricular rates is generally an even one. Odd ratios when they occur are usually solitary.

5. Auricular flutter is closely related to similar tachycardias of lesser rate on the one hand and to auricular fibrillation on the other. It may pass to one or the other. All such disturbances have a common pathology.

6. Impulses probably reach the junctional tissues in auricular fibrillation at rates exceeding 270 or 300 per minute.

7. Even when it has been present for many months, flutter may often be abolished by the administration of digitalis. This drug induces temporary fibrillation, and the normal rhythm is subsequently restored and may persist. But the administration of digitalis may be advisable, even when this full reaction cannot be obtained, for the purpose of reducing the ventricular rate.

8. The arterial curves when the auricles are in a state of flutter, are of very varied form. The pulse may be perfectly regular and slow or fast. Pulse irregularities which suggest the presence of extrasystoles or fibrillation are frequent. Often the full diagnosis may be made from these curves alone.

9. The venous curves are almost always obscure, on account of the weakness of the auricular systoles. When the pulse pauses are long the *a* waves may be distinct. Certain of the venous curves give an erroneous impression that a normal rhythm is present.

10. The electrocardiograms show auricular complexes which are contiguous at rates of 260-335 per minute. The line of curve never runs isoelectrically during ventricular diastole. As a rule, two auricular summits are seen for each ventricular, but under these circumstances alternate auricular representatives are easily overlooked. The auricular summits in lead *I* are small and pointed. In leads *II* and *III* they are extremely prominent, being equivalent as a rule to  $2 \times 10^{-4}$  or  $3 \times 10^{-4}$  volts; they may reach an equivalent of  $4 \times 10^{-4}$  volts; in these leads the complexes are convex. Together they form a continuous wavy or zig-zag line. The form of the *P* summits is very fairly constant from case to case, and the resemblance is often so exact as to suggest a definite and specific mechanism.

#### BIBLIOGRAPHY.

- <sup>1</sup> HERTZ AND GOODHART. *Quart. Journ. of Med.*, 1908-9, II, 213.
- <sup>2</sup> JOLLY AND RITCHIE. *Heart*, 1910-11, II, 177.
- <sup>3</sup> LEVY AND LEWIS. *Heart*, 1911-12, III, 99.
- <sup>4</sup> LEWIS. "The Mechanism of the Heart Beat," London, 1911.
- <sup>5</sup> LEWIS AND SCHLEITER. *Heart*, 1911-12, III, 173.
- <sup>6</sup> LEWIS AND GILDER. *Phil. Trans. roy. Soc.*, 1912, CCH, 351.
- <sup>7</sup> LEWIS. *Heart*, 1911-12, III, 279.
- <sup>8</sup> MACKENZIE. *Heart*, 1910-11, II, 378.
- <sup>9</sup> RIHL. *Zeitschr. f. exper. Pathol. u. Therap.*, 1911, IX, 496.
- <sup>10</sup> SAMOJLOFF. *Archiv. f. Anat. u. Physiol.*, 1907, *Phys. Abth.*, Sup. Bd., XXIX.
- <sup>11</sup> TURNBULL. *Heart*, 1911-12, III, 89.



Fig. 19 22  
of am  
mors  
right  
from  
are pr  
sec..

Fig. 23.

Fig. 24 20

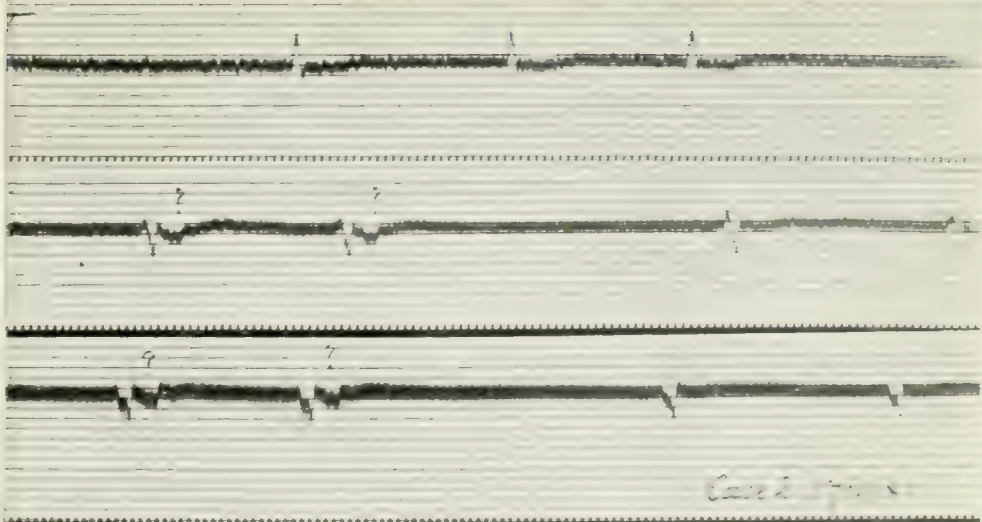


Fig. 25.

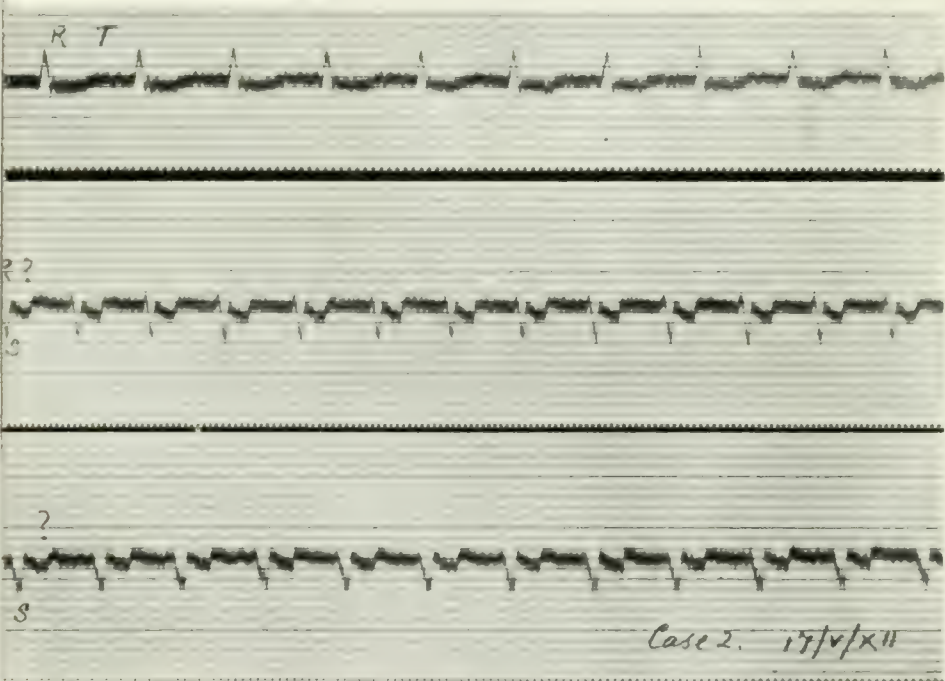


Fig. 26.

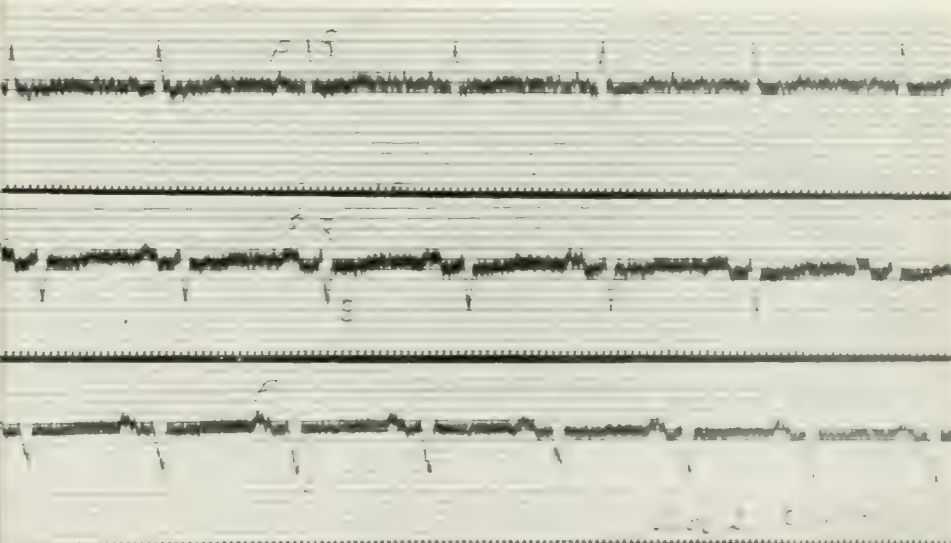
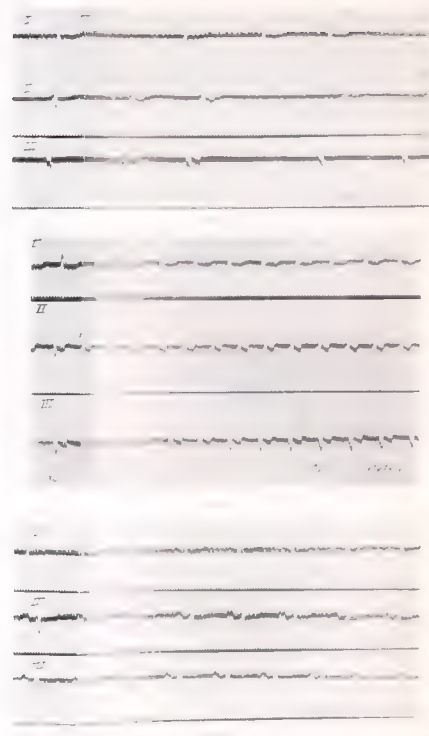
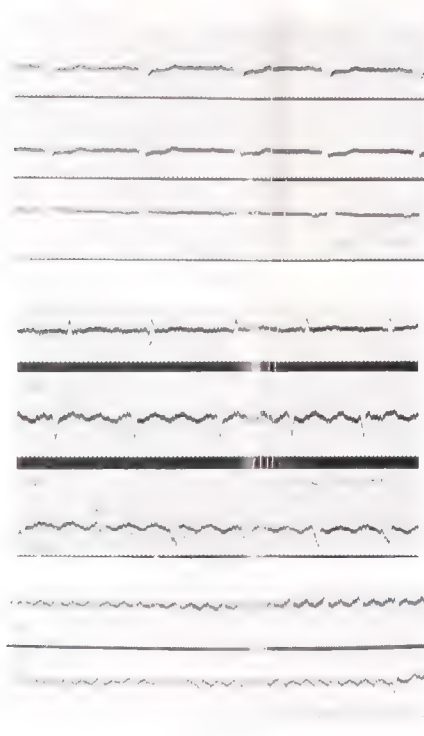
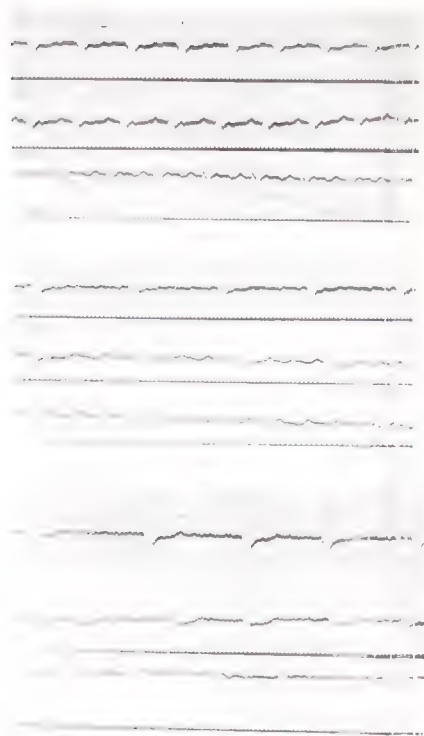


Fig. 27.





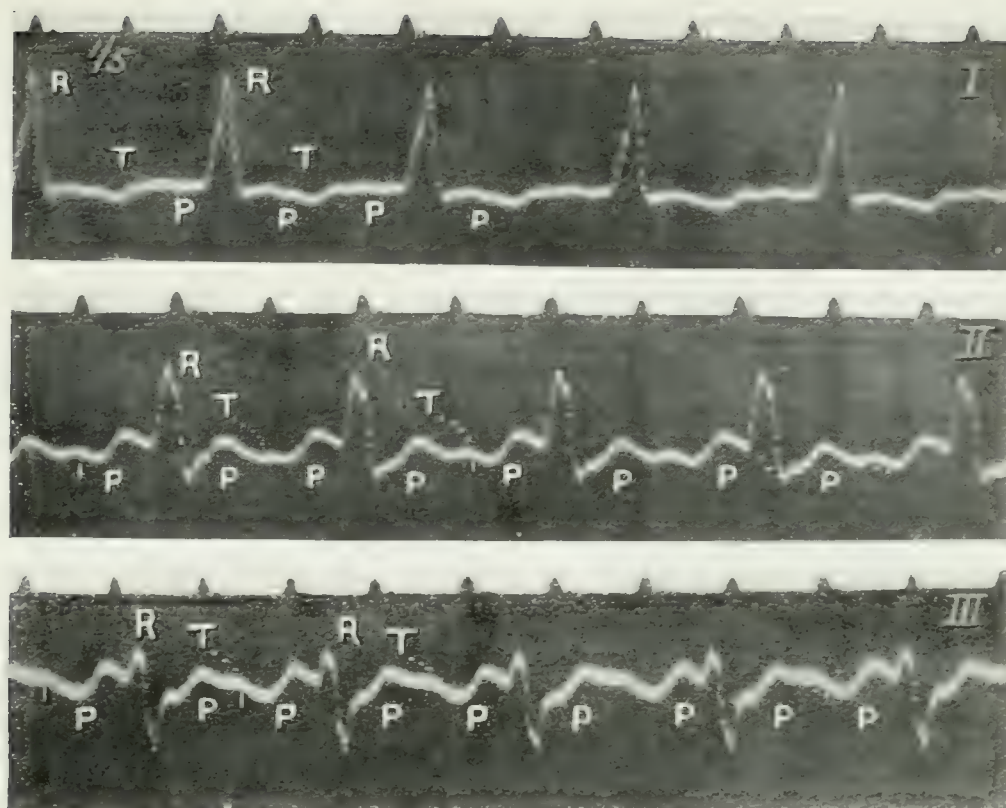


Fig. 35.

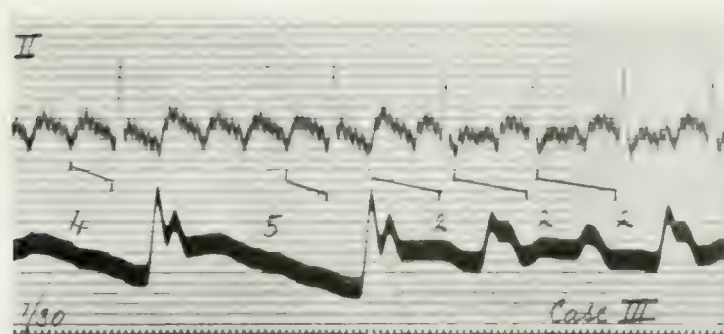


Fig. 36.

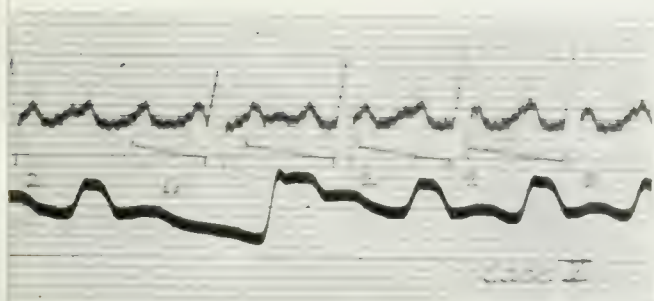
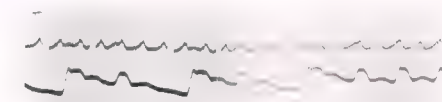
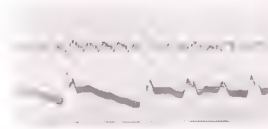
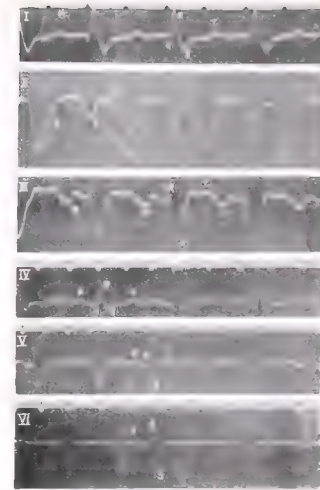
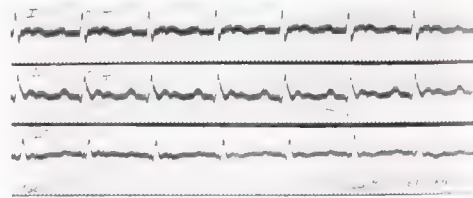
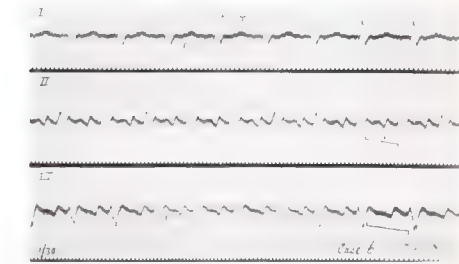
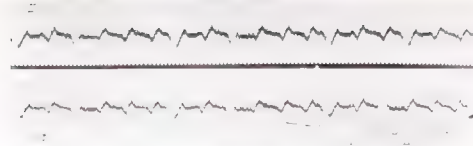
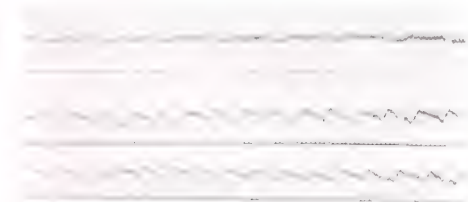
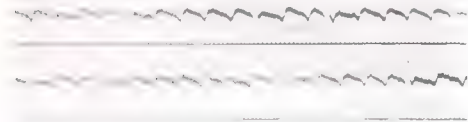
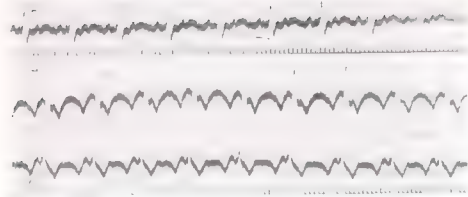


Fig. 37.





## THE POST-MORTEM EXAMINATION OF HORSES' HEARTS FROM CASES OF AURICULAR FIBRILLATION.

BY ALFRED E. COHN.

(*From the Hospital of the Rockefeller Institute for Medical Research*).

THIS report describes the histological findings of the hearts of three horses known to have been the subjects of auricular fibrillation. They were reported in this Journal by Dr. Th. Lewis.<sup>3</sup> The hearts were fixed in Müller-Formal (9-1), washed in running water, preserved in 70 per cent. alcohol and shipped to New York. The tissues supposed to contain the sino-auricular node and the septum of the heart containing the conduction system were excised. The latter, being too large a block to embed *in toto* was cut in slices about 3 mm. thick in a plane at right angles to the long axis of the heart. The slices and the sinus bearing areas were embedded in celloidin paraffin and cut in sections 10-15 micra thick. Every fifth section was mounted and stained with iron hæmatoxylin and Van Gieson's solution.

### *Heart from horse No. 1.*

This heart had been cut in pieces before I received it. The pieces supposed to contain the sino-auricular node were prepared in the manner described. Examination of the series showed that the node had not been included in the pieces excised. Inspection of the remaining portions of the heart, which had been sent with the excised pieces, showed that the area at the cavo-auricular junction at which the sino-auricular node is found had been cut in such a fashion that it appeared doubtful whether a successful reconstruction would be possible. After examining the sinus node of the other two hearts it was decided that further search for the sinus node in this horse would not be profitable.

The auriculo-ventricular node is found without trouble. It lies in a region well below the origin of the aorta. The central fibrous body of the human and canine heart is represented in horses, as in calves, by a cartilaginous structure. The node lies to the right of the central cartilage and is curved about its anterior extremity. In this horse it measures 3 mm. by 4 mm. in diameter. It has a distinct, well-developed auriculo-nodal junction, composed of fibres showing a transition from those forming the muscle of the auricle to those forming the muscle of the node. The auricular muscle requires no special description; it is similar to mammalian cardiac muscle. The structure of the A-V node offers certain peculiarities. It is formed of a meshwork of very coarse thick strands of connective tissue, supplied with a moderate number of nuclei. These meshes when magnified to about thirty diameters have proportions similar to fish netting. In the interstices of the

network, the muscle fibres of the node are found. These are like Purkinje cells, in the number and arrangement of their muscle fibrillæ, and in the character and number of their nuclei. The cells are probably larger than those seen in sheep and calves' hearts.

The *A-V* node is continued to the anterior aspect of the central cartilaginous body, and passes into the main stem which is exceedingly short, and which soon divides into a right and a left branch. The septum ventriculorum is almost entirely muscular at the level at which the beginning of the conduction system lies; an analogue of the septum membranaceum, as it exists in the human heart, was not found. It is within a thick muscular wall therefore that the division into right and left branches takes place. These are, relatively speaking, very small, showing only three or four cells side by side in cross section. As far as these were followed they lie within the muscular wall of the septum.

At the levels at which the main stem divides, Purkinje fibres are seen lying under the endocardium of both ventricles. These are undoubtedly the recurrent branches, which pass upwards to the base of the heart from the level of the papillary muscles, being continuous at that point with the arborisations of the right and left branches of the main stem.

No lesion, inflammatory or otherwise, was discovered in the course of the conduction system.

#### *Heart of horse No. 3.*

The area corresponding to the *sulcus (tænia) terminalis* was excised and was divided horizontally into two pieces, on account of its length. About five hundred sections (6,000 micra) were examined and the node was found in all of them. No abnormality was found in this node. To avoid repetition, a full description of this structure is postponed. That given for the heart of horse No. 5, in which the node is similar, may serve for both.

A description of the conduction system would duplicate that given for the heart of horse No. 1, and may therefore also be omitted.

#### *Heart of horse No. 5.*

*The sino auricular node.* The entire cavo-auricular junction of this heart was embedded. It included the circumference of the superior vena cava, the atrium below it, and the adjoining portions of both those walls of the right auricular appendix which unite to form its upper border. A block, 10 cm. deep, was cut into sections 10 micra thick, the plane of section being at right angles to the long axis of the vena cava. Every fifth section was mounted. It was found that this large piece had been so cut that it failed to contain the sinus node entirely. The lower levels of it were subsequently recovered in the portion of the anterior wall of the right auricular appendix lying to the right. No attempt has been made to calculate the size of the nodal tissue in these pieces. In the large piece the node was estimated to be 16.95 mm. (16,950 micra) long.



The upper extremity of the node is found in the wall of the right auricle above the entrance of the superior vena cava. It is embedded deep in the wall of the auricle midway between endocardium and pericardium. It gradually becomes differentiated from auricular muscle by the increase of connective tissue strands which appear among the muscle fibres. At a slightly lower level (1 mm.) the node assumes a more superficial position, lying 1 mm. from the pericardium. Its cross section is long and narrow, measuring 13 by 2 mm.. The pericardium over it is much thicker than elsewhere. There are many large nerves and numerous ganglia in its neighbourhood. There is no special large vessel, but there are numerous small ones.

At a slightly lower level, 1.5 mm. from the upper extremity, the node divides into two (tails), which may be designated as anterior (representing the structure which is usually seen) and posterior. This division occurs just a little above the entrance of the superior vena cava into auricle. Each of these tails of the node measures 8 by 1 mm. in cross section; they separate rapidly so that an interval between them, at first of 3 mm., rapidly widens to 16 mm., 0.7 mm. below the division. The space between these two portions of the node is formed of closely meshed and thin connective tissue which contains a moderate amount of fat. Here the anterior tail measures 10 by 0.5 mm., the posterior one, 5 by 2 mm.. Both are approximately triangular in outline. The posterior tail is 7.1 mm. in length from the point of division to its end. The anterior tail is 16.95 mm. in length, and at the lowest point at which its cross section is observed, measures 8 by 0.5 mm.

The node contains more connective tissue than the surrounding auricular muscle with which it communicates freely, but the amount is not abnormal. The muscle of which it is composed shows the usual interlacement, and the numerous nuclei, which are seen in this structure in other mammals; but the muscle fibres themselves are slightly thicker and are less striated. The fibres have no likeness to Purkinje cells. There is no evidence of abnormality with the exception of a small group of round cells near the lower extremity of the posterior tail of the node.

The occurrence of a bifid sinus node has been described by Schwartz<sup>5</sup> in the calf and sheep. When the sections of the heart of horse No. 3 were cut, two years ago, the pieces were not so large as those taken since that time. The nature of the divided sinus node therefore escaped observation. In the heart of horse No. 5 the structure of the node was similar to that found by Schwartz.<sup>5</sup> The node may be described as having the form of an inverted Y, the stem of which is short, and the anterior limb of the bifurcation being longer than the posterior.

The *auriculo-ventricular node* corresponds in general structure and in topography to that found in horse No. 1. A few details only need be added. In excising the piece of the septum of this heart containing the conducting apparatus, the coronary sinus was left intact. The relation of the auriculo-ventricular node to it can therefore be ascertained. It lies in the anterior lip of the coronary sinus and its upper border is a few millimetres posterior

to the line of attachment of the mesial cusp of the tricuspid valve. At this level the node measures 9 by 1 to 1.5 mm., a little lower it measures 11 by 2.25 mm., and lower still 9 by 1 mm..

The connective tissue meshes of the node in this, as in the other hearts, are only partly filled by muscle fibres. It is difficult to decide whether the spaces left are normal or are artifacts produced in the preparation of the sections. Opposed to the conclusion that they are artifacts is the unlikelyhood of Purkinje cells shrinking much when the surrounding ventricular muscle in the same section suffers little or at all. The Purkinje cells probably contain relatively more undifferentiated protoplasm than the muscle fibres, and this difference between them may render the deduction that one is unchanged because the other obviously is, unfair. If the spaces are not artifacts, they must be preformed. For this view there is some evidence. The spaces are lined with a membrane which presents slight nodular thickenings. These thickenings may represent cells, but they fail to show definite nuclear structure, at least with the dyes used in this investigation. Curran<sup>2</sup> would no doubt have identified these spaces with the bursæ he described. Another reason for thinking that such spaces are preformed is that they can all be filled by injecting fluid at a single appropriate place. This procedure has been successfully undertaken by Lhamon<sup>4</sup> and by the author.<sup>1</sup> It is probable that the spaces are preformed but their unusual size suggests shrinkage of the muscle cells within them.

The position, course, size and structure of the right and left branches are like those found in horse No. 1. No evidence of abnormality or of inflammation, old or recent, was observed.

#### *Summary and conclusions.*

The hearts of three horses, known to have suffered from complete irregularity of the heart, have been examined. In the first heart, the sino-auricular node was not found; in the other two, it showed no abnormality. The conduction system in all three hearts was intact and showed no lesion.

An arrangement of the sino-auricular node like that found in certain other mammals was observed in one of the hearts.

The auriculo-ventricular node, main stem and branches in these horses' hearts, are described in detail. They were free from abnormality.

#### BIBLIOGRAPHY.

- <sup>1</sup> COHN (A. E.). "Demonstration of Ox-Hearts showing injection of Conduction System." Proc. of the New York Pathol. Soc., 1911, XI, 130-132.
- <sup>2</sup> CURRAN (E. J.). "A constant bursa in relation with the bundle of His; with studies of the auricular connections of the bundle." Anat. Anziger., 1910, xxxv, 89-97; Anat. Record. 1909, III, 618-632.
- <sup>3</sup> LEWIS (TH.). "Irregularity of the heart's action in horses and its relationship to fibrillation of the auricles in experiment and to complete irregularity of the human heart." Heart, 1912, III, 161-171.
- <sup>4</sup> LHAMON (R. M.). "The sheath of the sino-ventricular bundle." Amer. Journ. of Anat. 1912, XIII, 55-70.
- <sup>5</sup> SCHWARTZ (G.). "Untersuchungen über das Sinusgebiet im Wiederkäuerherzen." Inaug.-Dissert., Berlin, 1910. Archiv. f. wissenschaft. u. prakt. Tierheilkunde, 1910, xxxvii, 152-179.



## OBSERVATIONS ON INJECTION SPECIMENS OF THE CONDUCTION SYSTEM IN OX HEARTS.

BY ALFRED E. COHN.

*(From the Hospital of the Rockefeller Institute for Medical Research).*

IN his preface to Tawara's monograph on the conduction system of the heart, Aschoff pointed out that in performing its orderly function, the region of the papillary muscles should contract before those of the base of the heart. He was able to prove from Tawara's investigations that the atrio-ventricular bundle was in reality distributed to this region first and only later to the base itself. These conclusions harmonised certain views of the embryology and the physiology of the heart with those put forward by Tawara concerning its structure. The method of investigating the anatomical pathway for conduction attained success only when serial sections of the heart were made and the system reconstructed. This method is tedious and the interpretation difficult. Numerous investigations attempted the method of gross dissection to lay bare the atrio-ventricular bundle, but satisfactory dissections of so complicated a system are quite impossible on account of the nature of the bundle and its ultimate distribution. For it is probable that no portion of the heart is free from a lining of conducting fibres, at least of Purkinje fibres, and these cannot be followed by the method of dissection. And since the origin of these fibres cannot be ascertained in this way, a theory of the distribution of the impulse to contraction cannot properly be constructed from the knowledge so gained.

A method by which the conducting system can be brought into view with ease and without subjecting it to trauma is by injection.\* Dyes were at first used as the injecting fluid. Some of the specimens demonstrated to the New York Pathological Society<sup>1</sup> were prepared in this manner. The stains that were used were all readily diffusible and were discarded on that account. Black india ink was then employed but was found to be too viscid to be a satisfactory medium, but india ink diluted with an equal part of water served the purpose very well. About twelve hearts in all were examined.

The ox hearts, of which photographs are shown (Fig. 1 and 2) were prepared in this way. After injection, these hearts were preserved in Kaiserling solution and have been kept as museum preparations. Lhamon<sup>2</sup> has published a photograph of the cavity of the left ventricle prepared in a

---

\* For the suggestion that an injection of the heart is possible the author is indebted to Dr. W. G. MacCallum. Dr. MacCallum had seen specimens so prepared in the summer of 1911 at Stanford University.

similar way but none of the right. The photograph now published of the left ventricle is in close agreement with his. A photograph of a successful injection of the right ventricle is now also reproduced.

It is not the intention of the present communication to discuss purely structural or histological matters. Lhamon<sup>2</sup> has made observations on these subjects which the author has been able to substantiate. It is the purpose of this communication to point out the clearness with which these injected specimens display the course and distribution of the impulse of conduction in the two ventricles.

In the left ventricle, three main branches have been named: one to the anterior, one to the posterior papillary muscle and one to the apex, the last issuing by two heads from the preceding branches. A comparison of these with the branches of the right ventricle will disclose a striking similarity in the general arrangement on the two sides. In the right ventricle one branch passes to the large anterior papillary muscle and to the venous base of the right ventricle, and one along the border of the large moderator band to the large septal papillary muscle, and to the conus arteriosus; the branch to the apex issues by separate heads from both the preceding. Thus the arrangement in the right ventricle is very like that of the left, but differs from it, in that the branches which are easy to identify as single strands on the left side, appear on the right broken into groups of branches, having a more extensive interlacement.

The gradual filling out of all these spaces in an orderly fashion is easily discernible during the progress of a successful injection. If the point of the fine injecting needle has been fortunately inserted in the left division of the bundle of the ventricle, the fluid can be seen to course parallelly along the three branches of the left division and to arrive at the papillary muscles first and a little later at the apex. The time relations are of course unreliable. But it is very important to notice that the injection of the papillary muscle takes place before that of the base, both venous and arterial. It is believed that inspection of the photograph demonstrates clearly that the injected pathways at the bases do not communicate with the left branch before division. They are in communication only with the branches supplied to papillary muscles; that is to say, the papillary muscles are supplied before either base or apex. This is the contention for which Aschoff argued. This method of distribution to the bases is true of the right ventricle as well as of the left.

Inspection during injection then shows that the papillary muscles are reached first by the fluid, and the bases and apex later. Whether the apex or one or the other base precede one another cannot be decided by this method; nor do the photographs aid in the decision; they show only the dependence of the basal portions on the papillary muscles for this distribution. Measurement of the relative length to each part from the origin of the left division may be useful in arriving at a solution, but such measurements have not been undertaken.



*Results and conclusion.*

Injection by diluted india ink is a valuable and simple method for demonstrating the course and relations of the conduction system in ox hearts. It has been shown that the injection reaches the papillary muscles first, and other portions later, notably the bases and apex ; and also that the branches of the system to these latter portions have no direct relationship with the main divisions or their principal branches. The basal and apical branches communicate with the principal branches at the papillary muscles.

The contention of Aschoff in respect of the course of conduction through the heart is therefore substantiated by this method of investigation.

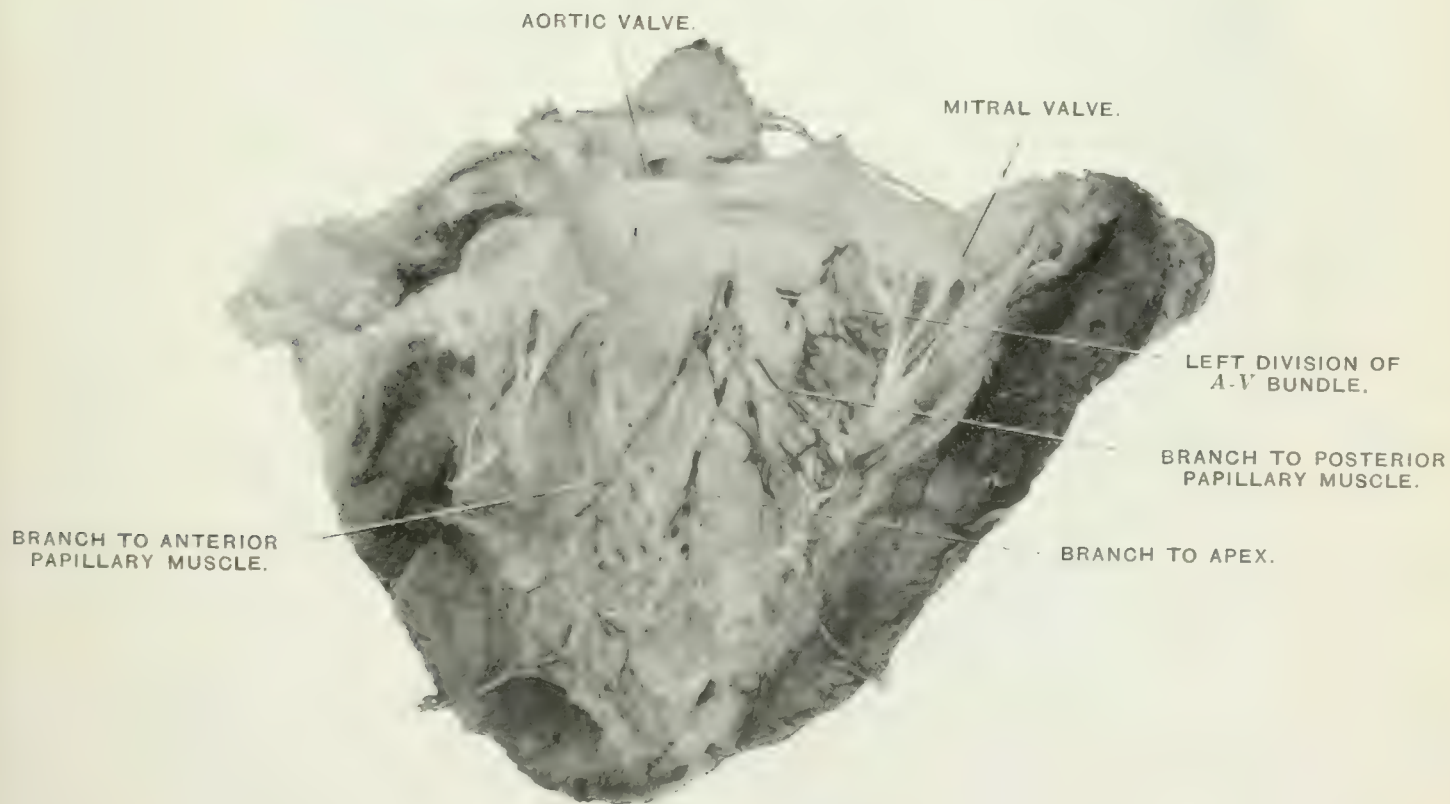
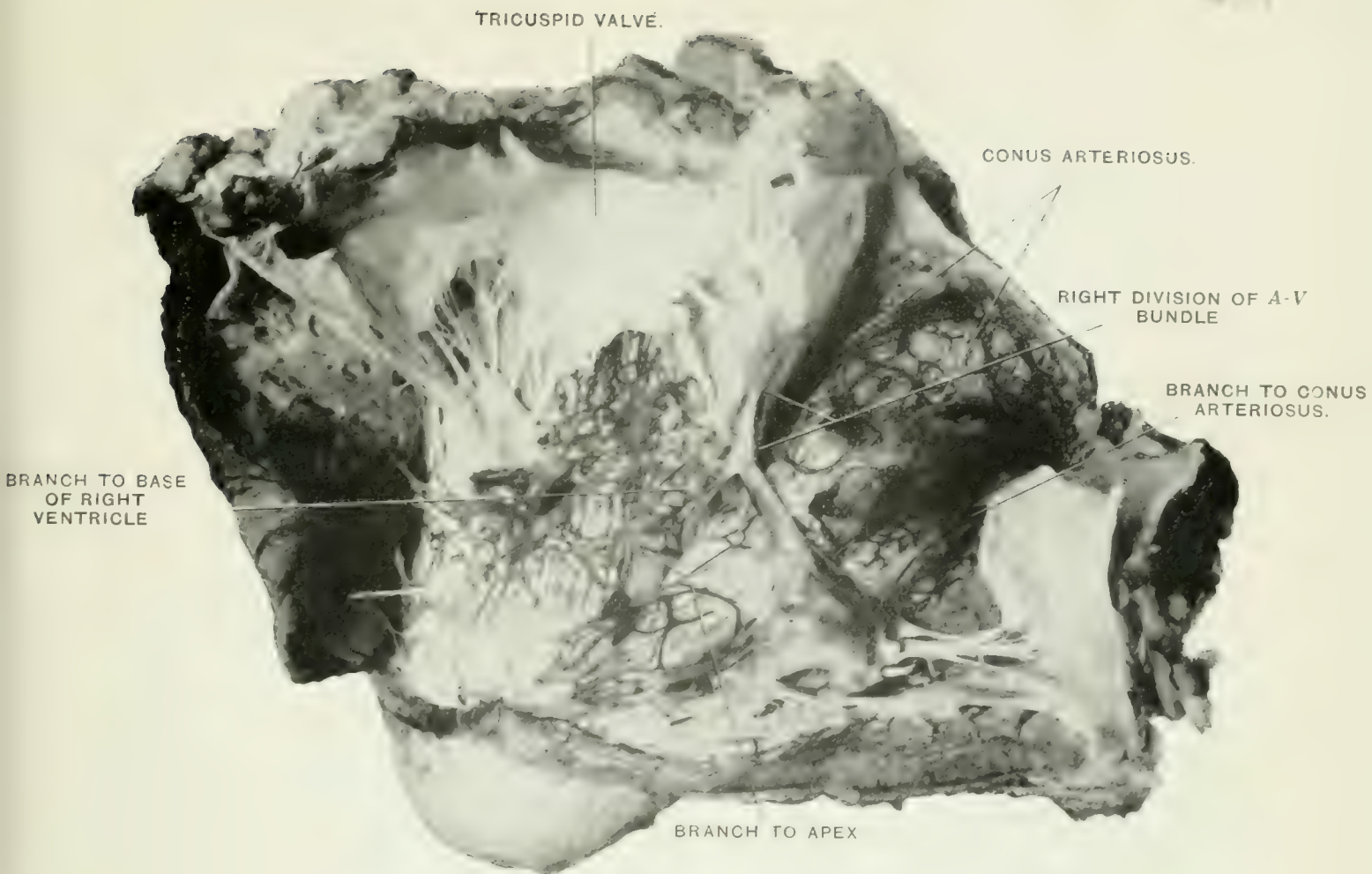
## BIBLIOGRAPHY.

- <sup>1</sup> COHN (A. E.). " Demonstration of Ox-Hearts showing injection of the Conduction System." *Proc. of the New York Pathol. Soc.*, 1911, *xi*, 130-132.
- <sup>2</sup> LHAMON (R. H.). " The sheath of the sino-ventricular bundle." *Amer. Journ. of Anat.*, 1912, *xiii*, 55-70.

Fig. 1. A photograph of the cavity of the left ventricle. Injection of the conduction system is shown.

Fig. 2. A photograph of the cavity of the right ventricle. Injection of the branches as in Fig. 1.









## FURTHER OBSERVATIONS UPON THE ISOLATED APEX PREPARATION IN THE FROG'S HEART.

BY G. H. CLARK AND WILLIAMINA ABEL.

(*From the Physiology Department of the University of Glasgow*).

### *I. Introduction.*

The work of Bernstein,<sup>2</sup> Bowditch<sup>3</sup> and others upon the isolated apex preparation in the heart of the frog showed that experimentally there is ground for the supposition that ganglion cells are absent in the lower two thirds of the frog's ventricle. The fact that Merunowicz<sup>7</sup> obtained rhythmic contraction when the heart was fed with certain fluids has been in large part explained by Gaskell<sup>6</sup> when he showed, by clamping the aorta, that if the pressure in the isolated apex is sufficient, contraction will result. Dogiel<sup>4</sup> and his co-workers<sup>5 & 8</sup> and Bethe<sup>1</sup> however, have described ganglion cells distributed extensively throughout the whole ventricle. Bernstein and Bowditch showed that when the apical two thirds are separated from the remaining third by crushing the intervening tissue it does not contract again even when an efficient blood supply is insured. Bowditch records instances where the apical segment was found days after the operation to be contracting along with the basal part of the heart. In subsequent experiments on these hearts he demonstrates experimentally by again crushing the ventricle still nearer the base that although the apex has apparently recovered from the first crushing which separated it from the base and is contracting on its own account, it becomes quiescent again after the second injury, thus proving that the apex has not originated impulses apart from those coming from the base of the heart. Bowditch concludes from his results that (1) the frog's apex does not possess the function of automatic motion; (2) resumption of contraction on the part of the apex is due to restoration of the imperfectly destroyed connection between apex and ventricle proper.

In these experiments no microscopic examination was made and consequently Bowditch's conclusions were not supported by histological evidence.

Bowditch's results appeared to us to require re-investigation and verification by histological methods and with the object of extending it in some measure we have undertaken the present investigation. We have further endeavoured to keep our animals alive for more prolonged periods

than Bowditch mentions, to allow of the possibility of more complete regeneration of nerve tissue.

## II. Methods.

The work was carried out in the following manner :—

To ascertain the distribution of nerve cells and fibres in the normal frog's heart longitudinal serial sections 7 micra in thickness were made, these sections were then stained by the hæmalum-eosin method which has been found very satisfactory for demonstrating ganglionic nerve cells in adult tissue. For comparative purposes the perfusion staining method was used, and several hearts were perfused with methylene blue 1 in 1,000, while others were perfused with 1 in 10,000. The osmic acid (rapid method) was tried in the case of two hearts but was not found to be very successful.

For the experimental work fifty frogs were used. The method of operation was as follows. The frogs were placed in a beaker of water to which ether had been added, and thus anæsthetised. They were then removed from the beaker and operated upon. An inverted V-shaped incision was made over the xiphi-sternum which was snipped through and folded back and the heart exposed. The pericardium was carefully opened, and the ventricle crushed transversely by a special pair of fine smooth forceps. The pressure exerted was in all cases sufficient to stop the transmission of impulses from the basal to the apical portions of the ventricle, no contraction being visible in the apical segment of the ventricle when the heart was returned to its normal position. The pericardium was stitched, the xiphi-sternum replaced and secured by a few stitches, and the skin wound stitched. The frogs were kept in a cool place supplied with a suitable amount of running water. *Rana temporaria* stood the operation well, but *Rana esculenta* did not. The frogs were kept for varying periods after operation; they were then pithed, the hearts exposed, and observations taken of the character and extent of their contraction. In cases where the apical segment was contracting, a further compression was applied completely across the ventricle or in the A-V groove. The object of this was to cut off from the contracting apical segment impulses coming from the base and the auricles and thus ascertaining if the origin of the apical contraction was intrinsic or extrinsic. After this had been done the hearts were placed in formaline fixative; washed and dehydrated in the ordinary manner, and embedded in paraffin. Longitudinal serial sections 7 micra in thickness were then made and stained by the hæmalum-eosin method.

## III. Results.

Some of the hearts were examined 24 hours after operation, and others at multiples of 24 hours.



1. *At 24 hours.* The animals all appeared healthy. As the conditions were exactly similar in all the hearts examined at this stage, a typical experiment is described. When the heart was exposed it was found pulsating regularly and apparently normally with the exception of the ventricular apex which was at rest. That the cavities of both the ventricular segments still remained patent was evident because the apical segment became dilated with blood forced into it during basal ventricular contraction. The sharp contractions elicited in the apical segment on mechanical stimulation made it evident that its excitability had been retained. These contractions, like those seen in the basal portion of the ventricle, were limited by the line of pressure.

Histological examination showed that muscular continuity was all but destroyed between apical and basal segments. The muscular tissues at the line of pressure were found to be lacerated, the laceration following a jagged irregular line.

2. *At 48 hours.* The hearts reacted in the same manner as those examined at 24 hours. On mechanical stimulation of the ventricular apex with a single stimulus the nature of the response varied with the relation of apical contraction to basal contraction. If the induced apical contraction coincided with basal contraction then the apical contraction lasted until the next basal contraction forced blood into the segment. On the other hand, if apical contraction coincided with basal dilatation then the apical segment became as usual dilated with blood during the ensuing basal contraction, but it again contracted before passing into the quiescent condition. Stimulation of the apical segment with a succession of stimuli showed the presence of a definite refractory period, while the rate of contraction was found to be slow as compared with other portions of the heart.

Histological examination showed injuries similar to those described 24 hours after operation. The line of pressure in the ventricle was marked by an irregular band of lacerated muscular tissue mixed with hæmorrhagic patches.

3. *At 72 hours.* With the exception of one heart the experiments yielded the same results as at 24 and 48 hours.

In one heart exposed at this period contractions were clearly seen in both apical and basal segments of the ventricle. These contractions began on the left side immediately below the auriculo-ventricular groove, passed to the right side, then downwards to the right side of the apical segment, and finally upwards to terminate in the left side of the apical segment at the seat of injury. A narrow non-pulsating band extended half way across the ventricle on the left side. The pulsations just described started above this

narrow band on the left side and following the circular route described, finished below it. This non-pulsating band represented a portion of the line of pressure and formed an effectual bar against the progress of impulses downwards from the left basal portion of the ventricle to the left apical portion.

Histological examination showed that the muscle in the portion of the ventricle which did not contract was completely lacerated. The remainder of the line of pressure could be recognised and at many points in the serial sections complete muscular continuity could be traced between the basal and apical ventricular segments.

4. *At 96 hours.* The conditions already described as being found at the earlier stages were also found at this stage.

When the hearts were exposed pulsations were seen to be strictly limited to those portions of the hearts proximal to the lines of pressure, while the apical segments were in all cases quiescent. The apical segments still retained their excitability and responded promptly to stimuli.

Histological examination of a typical heart at this stage showed complete laceration of the muscular tissue along the line of pressure.

5. *At 120 hours.* The hearts examined at this stage showed precisely the same phenomena. The apical segment in each case was seen to be at rest; its excitability was, as usual, retained and when stimulated with a tetanising current a rhythm of about 6 contractions in the 30 seconds was demonstrated.

Histological examination of serial sections through the hearts showed complete laceration of the muscular tissue between the basal and apical ventricular segments.

6. *At 144 hours.* In each case the apical segment of the heart was found to be at rest, and reacted as at earlier times. In one case the apical rhythm was found to be 14 beats in 30 seconds in response to the interrupted current, during the same period the basal ventricular segment contracted 34 times.

Histological examination of this heart showed complete laceration of the muscular tissue along the line of pressure.

7. *At 168 hours.* With one exception these hearts showed the same phenomena as at the earlier times.

In this case the whole heart was actively pulsating. There was, however, a short pause in the progress of contraction over the ventricle, occurring at the junction of the middle and lower thirds, that is at the line of pressure. The further experiment of squeezing the ventricle transversely between the auriculo-ventricular groove and this line was undertaken, with the result



that the whole of the ventricle distal to the second line of pressure stopped pulsating. The large apical segment thus isolated was seen to dilate on contraction of the basal ventricular segment in the way described before. The apical segment was excitable and contracted sharply on stimulation, the contraction being limited by this second line of pressure. If stimulated with the induced current it contracted, but immediately after this contraction a wave of inhibition spread over the whole heart. The auriculo-ventricular groove was now crushed with the result that the basal ventricular segment, lying between the auriculo-ventricular groove and the second line of pressure, continued pulsating, but at a slower rate than the auricular portion of the heart. A comparative count showed the basal ventricular rhythm to be 7 beats per 30 seconds, while the auricular rhythm was 19 beats per 30 seconds.

Histological examination showed that the original line of injury had not completely separated the apical from the basal segment. Along the second line of pressure the extent of the injury was somewhat masked by hæmorrhage. At the auriculo-ventricular groove the pressure exerted had not been sufficient to cause severe laceration of the tissues. Many of the cells of Bidder's ganglion had escaped injury.

In another frog examined at the same stage after operation the apical segment was found to be at rest. It displayed the usual phenomena of the resting apical segment, which have already been described.

8. *At 192 hours.* One heart showed a variation from the quiescent apex condition.

When the heart was exposed pulsations were seen over the entire ventricle. The line of pressure was seen as a faint scar-like band, but there was no appreciable delay of the conduction at this point. The ventricle was again crushed transversely between the first line of pressure and the auriculo-ventricular groove. The portion of the ventricle distal to the second line of pressure did not stop beating but slowed considerably. Observation showed that a pulsation of the basal ventricular portion was occasionally conducted over the second line of pressure into the apical segment. The ratio of pulsations was found to be 16 per 30 seconds in the basal segment, and 5 per 30 seconds in the apical segment. Pressure was next applied along the auriculo-ventricular groove. The ventricles stopped beating although they readily contracted when stimulated mechanically. The contractions induced by stimulation below the auriculo-ventricular groove spread over the entire ventricle. Pressure was again applied along the second line of pressure, and it was found that contractions induced in the ventricle proximal or distal to this line were now effectually blocked. The first pressure applied had evidently not been sufficient to destroy all the connections between the ventricular segments.

Histologically the primary line of pressure was easily recognised, but the injury to the muscular coat was comparatively slight and no difficulty

was found in tracing strong muscular bands across the line of injury. The second line of pressure was masked by a considerable amount of hæmorrhage and the extent of injury was not clearly seen.

9. *At 216 hours.* The hearts of the frogs examined were found to be actively pulsating with the exception of the apical segments which were in all cases quiescent and responded in the usual way to stimuli. In one case pressure was applied along the auriculo-ventricular groove with the result that for 2-3 minutes pulsations ceased over the entire ventricle. Stimulation of the basal portion of the ventricle during this period elicited contractions which in some few cases spread over to the apical segment distal to the original line of pressure. Pressure was now applied along the original line of pressure. The auricles and basal portion of the ventricles now gave 5 beats per 30 seconds while the apical segment gave 2 per 30 seconds. Observation was maintained for some time but the apical contractions although very slow did not disappear.

Histological examination showed that along the original line of pressure laceration of the tissues had been very extensive. Careful examination of the area failed to discover any direct muscular continuity between the segments of the ventricle. The fact that this area was twice subjected to pressure before examination, made it impossible to determine the degree of injury after the first pressure. Slight muscular continuity may have existed between the segments prior to pressure being applied for the second time.

At the auriculo-ventricular groove a considerable amount of laceration of the tissues had occurred but not sufficient to separate completely the auricles from the ventricle.

10. *At 240 hours.* All the hearts showed the quiescent apex. Additional observations were made on one heart. It was found that when pressure was applied along the auriculo-ventricular groove a contraction immediately succeeded by dilatation swept over the *entire* ventricle. Pressure was next applied between the auriculo-ventricular groove and the operative line of pressure and again a wave of contraction followed by dilatation swept over the heart. After this passed it was seen that the apical segment distal to the third line of pressure had stopped contracting while pulsations continued in the basal ventricular segment. Histological examination of this heart showed complete separation of the muscular tissue along the operative line of pressure. Along both the second and third lines hæmorrhage masked the appearances so that it was impossible to ascertain exactly the extent of injury.

11. *At 264 hours.* The apical segments were in each case quiescent and displayed the usual characteristics. The following observations were made on one heart. Pressure was made along the auriculo-ventricular groove with the result that absolute stoppage of movement occurred over



the auricles and basal portion of the ventricle. The basal ventricular segment gradually resumed pulsation and was followed a little later by the auricles. After a short time the normal rhythm of auricles and ventricles was resumed. It was also noticed that stimulation applied to the apical segment, after pressure had been applied along the auriculo-ventricular groove, sometimes resulted in a contraction which spread upwards to the basal portion of the ventricle beyond the original line of pressure.

Histologically no muscular continuity was found between the basal and apical ventricular segments separated by the original line of pressure. At the auriculo-ventricular groove the injury to the tissues was not sufficient to separate completely auricles from ventricle.

12. Two frogs survived operation for four weeks. When the hearts were exposed the ventricular apex was found in both cases to be quiescent. The line of pressure was easily recognised, while both apical segments presented a somewhat shrivelled appearance. Histological examination of one heart showed complete alteration in the structure and appearance of the muscle of the apical segment. Along the line of pressure and distal to it were numerous fibroblasts, while the muscular tissue of the apex was replaced almost completely by fibrous tissue.

13. In one case a frog lived six weeks after operation. When the heart was exposed the same condition as that described at four weeks was found. The apical segment was, however, very much shrivelled, while the line of pressure was recognised as a cicatricial band along the most distal portion of the pulsating segment of the ventricle. On histological examination it was found that the apical segment was composed of fibrous tissue which had almost completely replaced the muscular tissue.

#### *IV. Discussion of results.*

It is evident that pressure applied transversely to the ventricle may be sufficient to prevent the propagation of contraction from one portion of the ventricle to another as shown by Gaskell and others. This block may be partial or temporary, as is shown where on examination of the hearts at different periods after operation, contractions are seen passing to the apical segment across a portion of the line along which pressure had been applied, or across the whole length of this line with little or no delay. Histological examination shows definitely that in these instances the muscular tissue of a segment of the line of pressure has escaped severe injury and serves as a link between the basal and apical segments transmitting contractions. In other cases the muscular tissue along the whole line of pressure has escaped severe

injury with the result that transmission of contractions is little if at all interfered with.

In most of the cases, however, the apical segment distal to the line of pressure does not beat again and this is shown histologically to be associated with complete or all but complete laceration of the muscular tissue along this line. In all cases the pressure exerted on the ventricle at the time of operation was sufficient to cause cessation of contraction in the apical segment.

Where the frogs survive the operation for four and six weeks the apical segment in addition to being quiescent has undergone a degenerative change appreciable to the naked eye by its shrivelled appearance, and histologically by the substitution of fibrous for the muscular tissue of the segment.

Up to eleven days after operation the excitability of the apical segment is retained.

Mechanical or electrical stimulation promptly elicits contractions which are limited, in the case of quiescent apical segments, by the line of pressure. These contractions may be elicited so as to demonstrate a definite rhythm which varies in different animals and bears no relationship to the rhythm of the basal portion of the ventricle.

When contraction of the apical segment is mechanically induced so as to synchronise with the contraction of the basal segment the blood is forced out of the whole heart and the apical segment remains contracted until the basal dilatation has distended that part with blood. Basal contraction now forcibly dilates the apex with blood and the apex does not contract. Where apical contraction coincides with basal dilatation, the subsequent basal contraction fills the apical segment with blood, and the sudden great increase of pressure in the apical part acts as a sufficient stimulus to cause a further single apical contraction.

In an instance where a heart was examined nine days after operation, while the apical segment was quiescent when exposed, yet after pressure had been applied along the auriculo-ventricular groove stimulation of the basal portion of the ventricle was sometimes followed by a wave of contraction spreading to the apical segment. Pressure made along the original line of pressure was followed by a slowly recurring pulsation of two beats in thirty seconds in the apical segment.

In a heart examined ten days after operation a wave of contraction was seen to pass over the whole heart, apical segment included, on pressure being made along the auriculo-ventricular groove and midway between it and the original line of pressure. But no resumption of pulsation was seen in the apical segment. Further, in a heart examined after eleven days and in which the apical segment was quiescent, it was found that stimulation of this segment after pressure had been made along the auriculo-ventricular line was sometimes followed by a contraction which spread upwards to the basal segment. In all these cases histological examination showed no



muscular continuity between the basal and apical ventricular segments. The contraction seen in the apical segment of the heart after nine days was evidently not due to an intra-apical nerve mechanism since it was only produced after pressure had been applied to certain other parts of the heart ; in the second case the wave of contraction, described as occurring in the apical segment, was momentary and associated with severe pressure. In a third case there was spread of contraction induced in the apical segment to the basal ventricular segment after auriculo-ventricular pressure. Although these three cases are recorded in frogs kept nine, ten, and eleven days after operation, the conditions are not characteristic of all hearts at these periods after operation ; it seems probable that the phenomena described are due to fibrous connections or to mechanical factors such as changes in ventricular pressure induced by pressure along the auriculo-ventricular groove. Pressure applied along the auriculo-ventricular groove in the case of hearts examined from one to eight days after operation is in no case followed by any such phenomena.

#### SUMMARY.

1. When the apical two-thirds of the ventricle is completely separated from the basal third as proved by histological examination, no recurrence of apical contraction takes place.
2. When the apex contracts after being separated from the basal segment by a line of crush, histological examination shows that muscular continuity has not been completely destroyed.
3. In three instances severe pressure applied at the A-V groove some time after the operation caused a series of contractions of the whole heart.
4. In hearts left for periods of four and six weeks the muscular tissue of the apical segment was largely replaced by fibrous tissue.

The experimental part of this work was done by Dr. G. H. Clark. We acknowledge our deep indebtedness to Professor Noël Paton for guidance and encouragement in the work.

A grant was received from the Carnegie Trust to defray the expenses of this research.

## BIBLIOGRAPHY.

- <sup>1</sup> BETHE. "Allgem. Anat. u. Physiol. des Nervensystems." Leipzig, 1903.
- <sup>2</sup> BERNSTEIN. Centralblt. f. d. med. Wissenschaften, 1876, xiv, 385.
- <sup>3</sup> BOWDITCH. Journ. of Physiol., 1878-9, i, 104.
- <sup>4</sup> DOGIEL. Archiv. f. d. ges. Physiol., 1910, cxxxv, 1.
- <sup>5</sup> DOGIEL U. ARCHENGELSKY. Archiv. f. d. ges. Physiol., 1906, cxiii, 1.
- <sup>6</sup> GASKELL. Journ. of Physiol., 1880-82, iii, 51.
- <sup>7</sup> MERUNOWICZ. Ber. d. k. Sächs. Gesellsch. d. Wissensch., Leipzig, 1875, xxvii, 252.
- <sup>8</sup> TUMÄNZEW U. DOGIEL. Archiv. f. mikr. Anat. 1890, xxxvi, 483.



# THE TIME RELATIONS OF HEART SOUNDS AND MURMURS, WITH SPECIAL REFERENCE TO THE ACOUSTIC SIGNS IN MITRAL STENOSIS.

By THOMAS LEWIS.\*

(From the Cardiographic Department, University College Hospital  
Medical School).

## *Method.*

IN any present day investigation in which the time relations of events in the human heart cycle are studied, the electrocardiogram is the most accurate standard of reference. In choosing this method of timing the heart sounds, I follow the lead of Kahn,<sup>13</sup> Fahr<sup>7</sup> and others; but in preference to uniting heart sounds and electrocardiograms and subsequently unravelling the combined picture, the less laborious and more accurate method, recently adopted by Bull,<sup>1</sup> of recording the two pictures separately and simultaneously on a single photographic plate has been employed.

For the electrocardiograms, the usual installation has been utilised, and the curves have been taken from the oblique lead, the right arm and the left leg. This lead has been chosen because in standard curves the average excursion is greatest and because *T* is usually a prominent and upwardly directed summit.

To record the heart sounds I have adopted the method of Einthoven,<sup>1</sup> utilising a second string galvanometer and projecting the images of the two strings, side by side, upon the same camera. The heart-sound galvanometer is connected to the secondary coil of a simple transformer (5,300 ohms.), whose primary coil (10 ohms.) is in series with a graduated resistance (70 ohms.), a microphone and cell. The microphone receiver consists of the chest piece of a stethoscope joined to the microphone by a short length of thick-walled rubber tubing, the latter having a side opening communicating freely with the air of the room. The electrocardiographic curves are taken with the string at such a sensitivity as to yield an excursion of 3 cm. to 3 millivolts, the usual amplitude. The tension of the second, or heart-sound string, is greater, giving a deflection of only 1 cm. to 4 millivolts when sounds of normal intensity are recorded.† In cases of mitral stenosis the apical sounds are so intense that a tighter string is sometimes employed. No attempt has been

---

\* Aided by a grant from the British Medical Association. A preliminary notice of this work appeared in the *British Medical Journal*, December, 1912.

† The deflection time of the string is then about .004 seconds for 1 centimetre excursion.

made to standardise the amplitude of the sound record, for, in the first place, different standards would be required for different types of case, and, in the second place, it has been found impracticable, so far, to keep the factors constant. Displacement of the chest receiver a fraction of an inch to one or other side, and especially change in the pressure with which the receiver is applied to the chest wall, profoundly affect the amplitude of the sound record. So, as the primary object of the work was to investigate the time-relations of the auscultatory signs, the excursion was arranged so as to be convenient for measurement. As has been stated, in taking records of the intense apical sounds of mitral stenosis a smaller sensitivity has been employed. It is possible therefore that in this condition certain of the smaller sound vibrations escape detection, but, as will be seen, this possibility does not materially affect the final conclusions.

The transmission delay of the phono-electrocardiograph has been calculated by simultaneously recording the sound and current yielded by a simple contract. It amounts to  $\cdot 002$  seconds, an almost negligible quantity; this quantity has been allowed for in the tables which follow. For all practical purposes the records may be regarded as simultaneous.

The primary object of the work has been the study of the position of the diastolic murmurs in mitral stenosis, relative to other cardiac events; but in pursuing this subject it was considered desirable to study further the relation of the electrocardiograph to the heart sounds in the normal subject.

*The normal heart sounds, their relation to the electrocardiogram, and the relation of both to systole of the ventricle.*

The standard chosen being the electrocardiogram, our previous knowledge of its time relations to other cardiac events may be summed up. Kahn<sup>13</sup> recorded the rise of pressure in the left ventricle as beginning at the end of the summit *R* in dogs. In curves from the muscle of the ventricle he found the first indication of contraction  $0\cdot 031$ - $0\cdot 035$  seconds after the beginning of *R*\* (about  $1/100$  seconds earlier than the estimate for the rise of pressure). He concludes that the mechanical shortening of the front of the right ventricular wall begins at the least  $0\cdot 03$  seconds later than the upstroke of *R* (lead *II*), but for several reasons he is of opinion that the interval between *R* and the commencement of the contraction in the deeper lying muscle is much less than this interval. My own measurements for dogs, taken in a similar fashion, agree; in these the shortening of the ventricular wall commences between  $\cdot 030$ - $\cdot 033$  seconds after *R*, where this peak opens the ventricular electrocardiogram.

The most satisfactory comparison for our present purposes, and the only one in man, is that between electrocardiogram and heart sounds. It places the commencement of contraction earlier.

---

\* The total duration of *R* is variable but may be stated as usually reaching three or four hundredths of a second.



Kahn finds the commencement of the first sound with, or .01 seconds before, the end of *R*. Fahr,<sup>7</sup> using superimposed records which were particularly clear and accurate, places it earlier and finds that it usually precedes *the summit of R* by .01 seconds, though it may be with or slightly beyond this point. Fahr laid especial emphasis upon small initial sound vibrations which were obscured in Kahn's records.

The second sound is found by Kahn to fall approximately .03 seconds after the end of *T*, while Fahr makes the same interval .01-.02 or even less.

TABLE I.

|          | Heart rate. | Beginning of <i>Q</i> to 1st sound.* | Beginning of <i>R</i> to 1st sound. | Length of 1st sound. | End of <i>T</i> to 2nd sound.* | Length of 2nd sound. | Frequency of Vibration. |            |
|----------|-------------|--------------------------------------|-------------------------------------|----------------------|--------------------------------|----------------------|-------------------------|------------|
|          |             |                                      |                                     |                      |                                |                      | 1st sound.              | 2nd sound. |
| D.       | 77          | 0.039                                | 0.026                               | 0.13                 | 0.0                            | 0.09                 | 68                      | 50         |
| P. C. G. | 77          | 0.036                                | 0.026                               | —                    | - 0.015                        | —                    | 45                      | 64         |
| T.       | 74          | No <i>Q</i>                          | 0.009                               | 0.15                 | - 0.014                        | 0.11                 | 54                      | 54         |
| W. H.    | 100         | 0.015                                | 0.008                               | 0.16                 | 0.0                            | 0.12                 | 53                      | 65         |
| J. R. Y. | 95          | No <i>Q</i>                          | 0.005                               | 0.19                 | 0.002                          | 0.08                 | 59                      | 43         |
| A. P.    | 108         | 0.012                                | 0.006                               | 0.14                 | 0.005                          | —                    | 58                      | 53         |
| W. J. P. | 75          | No <i>Q</i>                          | 0.015                               | 0.14                 | 0.0                            | 0.07                 | 68                      | 64         |
| G. R. M. | 68          | 0.015                                | 0.005                               | 0.15                 | —                              | 0.08                 | 47                      | 63         |
| J.       | 81          | 0.011                                | 0.002                               | 0.13                 | —                              | —                    | 61                      | 68         |
| P.       | 72          | 0.024                                | 0.011                               | 0.14                 | 0.005                          | 0.07                 | 57                      | 50         |
| F.       | 102         | No <i>Q</i>                          | 0.026                               | 0.12                 | 0.0                            | 0.09                 | 50                      | 86         |
| T. L.    | 90          | 0.028                                | 0.018                               | 0.13                 | - 0.013                        | 0.08                 | 48                      | 40         |
| L. L.    | 78          | 0.013                                | 0.008                               | 0.15                 | 0.019                          | 0.13                 | 57                      | 40         |
| G. S.    | 90          | 0.025                                | 0.018                               | 0.14                 | 0.028                          | 0.09                 | 70                      | 62         |
| H.       | 75          | 0.030                                | 0.025                               | 0.13                 | - 0.035                        | 0.07                 | 61                      | 43         |

\* So far as the commencement of sounds is concerned the error is probably not greater than .005 seconds. The variability in the length of sounds introduces a larger error in the corresponding measurements.

My own heart sound curves were taken from 23 young male subjects; the curves in 15 of these were relatively free from extraneous sound vibrations, and the measurements are given in Table I, from which all data have been excluded where the initial sound vibrations were not clearly distinguishable. The measurements were made upon the original curve magnified some thirty diameters upon an epidiascopic screen; each figure in the table is an average of three measurements.

The measurements of Table I are in agreement with those of Fahr. The first sound begins from  $\cdot 002$  to  $\cdot 026$  sec. after the commencement of  $R$ , or from  $\cdot 011$  to  $\cdot 039$  sec. after the commencement of  $Q$ . The second sound is also variable in position in relation to the end of  $T$ , but seems often to be earlier than has hitherto been supposed. It may start as much as  $\cdot 035$  sec. before the end of  $T$  or it may be as late as  $\cdot 028$  sec. after the end of  $T$ . As a rule it begins at the end of  $T$  or within a hundredth of a second of it.

Thus there is general agreement that the earliest sign of contraction in the ventricle (other than the electrocardiographic), namely the commencement of the first sound, occurs from one to three hundredths of a second later than the commencement of  $R$ . We may take two hundredths as an average and the instant arrived at will represent the commencement of systole with a greatest error of two hundredths of a second. Similarly the end of systole may be taken as occurring where  $T$  meets the base line, and the error is no greater than three hundredths of a second. Usually the errors will be much smaller. An electrocardiogram, in which the summits of  $R$  and  $T$  are conspicuous, is therefore an extremely valuable standard from which the onset and offset of systole may be estimated. Examples of normal heart sounds are shown in Fig. 1.

*The third heart sound.* A third heart sound was discovered by A. G. Gibson<sup>11</sup> a few years ago, and Einthoven<sup>4</sup> found it in records from normal subjects. It is a dull and distant sound, occurring for the most part when the heart beats slowly; it is audible and can be recorded over only a relatively small percentage of hearts. Einthoven's measurement placed its commencement at a distance of  $\cdot 13$  seconds from the commencement of the second sound. My own collection of normal curves contains only a single notable example of it (Fig. 2); in this instance it also lies  $\cdot 13$  seconds from the second sound and consists of a single and complete vibration; a trace of a similar sound is found in several other curves of the normal series (see Fig. 1).

#### *Acoustic signs in mitral stenosis.*

The murmurs of mitral stenosis vary both in character and in their time relations to other events of the cardiac cycle. In the first place we may examine the simple murmurs which are associated with a regular heart action and a normal sequence of chamber contraction.

*The time relation of the so-called presystolic murmur.* It has been an almost universal custom to term the common murmur, which characterises mitral stenosis, the *presystolic murmur*, but it is probable that it is generally recognised at the bedside not so much by its position in the cycle as by its character. Called presystolic, it is generally believed to be presystolic in time; yet from time to time its actual position in the cycle has been hotly contested. I do not propose to pursue a discussion, which at the advent of



sound records has become almost purely historical.\* Let us take a series of patients presenting themselves at a general out-patient department with signs of mitral stenosis, and sort from them those whose hearts beat regularly and in whom we hear at the apex beat a low pitched rasping murmur which leads up to a loud ringing sound. The murmur will be accompanied as a rule by a palpable thrill. These cases will form the greatest part of the whole series; the signs are those of a funnel shaped or "button-hole" orifice. The first question which we will ask of the phonogram is the relation of this murmur to the other events of the cardiac cycle.

I have taken ten such cases and the analyses of the curves are to be found in Table II. Records of the sounds were obtained at two points: (1) a low point near the nipple line at which the murmur was loudest and where it tended to be localised (apical curve), and (2) the nearest point to the apical one at which no trace of such murmur could be heard and, for preference, at which both first and second sounds were clearly audible (control curve). These points have naturally varied: the first lying in the fourth, fifth or sixth interspace, three, four or five inches from the mid-line; the second lying in the same spaces nearer the middle line, over the ensiform cartilage or at times in the third left interspace. The object has been to compare, so far as possible, the relations of the murmur, not only to the electrocardiogram, but also to the first and second sound in the same case (see Fig. 3 and 4). In the apical column of Table II, I give the length of the gap between second sound and murmur, the length of murmur + first sound (or, where there is no gap, the total length of second sound, murmur and first sound), and lastly the interval between the beginning of the murmur and *R*. In the control column, I give the position of the first and second sounds and their lengths; and also the length of the murmur, as calculated by subtracting the length of first sound, or first and second sound as the case may be, from the totals in the apical column. In this manner and by a careful comparison of the two curves, the first and second sounds in what is termed the apical curve may usually be identified with considerable accuracy, and the second sound, murmur and first sound in a given cycle may be mapped out. Comparing the position of the first sound in the control curve and that of murmur + first sound in the apical curve, the combined sound is naturally the longer, and the lengthening is always the result of an extension towards presystole.

The relations have been constant in one respect; the apical curve shows a sound of considerable amplitude running up to the first sound. A murmur having generally a rather greater vibration frequency† than has

---

\* Other workers have recorded this murmur<sup>17</sup>; but the records obtained have not been easy to decipher.

† The frequency of vibration of the first sound is in my normal series from 45 to 70 per second, of the second sound from 40 to 86, while that of the murmur is from 41 to 107 per second, the averages being, first sound 57.0, second sound 56.3 and murmur 68.5 (see Tables). The measurements included all the vibrations corresponding to sound or murmur. I use the sounds of the normal curve in preference to those of the mitral stenosis cases, because the latter are so often complicated by systolic murmur vibrations. The frequencies of the sounds in the mitral stenosis series are given in Table II.

the first sound is seen to occupy the period directly preceding the first sound in the same case. So far, it may be rightly termed a presystolic murmur. Its relation to the electrocardiogram is the expected one. The first sound in these cases occupies similar positions to the normal, as may be seen in the tables; it commences from two to four hundredths of a second after the commencement of *R*; it may be a little further away from *R* than in normal cases, at the most by one or two hundredths of a second, but not more so than is fully accounted for by the loss of the initial vibrations; these necessarily cannot be discovered except they are preceded by a steady line.\*

Tracing it backwards, the murmur lies opposite the upstroke of *R* and opposite the electric complex which represents the contraction of the auricle. How far back does it extend? This is variable, according to the length of the murmur and the length of diastole. In half the cases tabulated the end of the second sound and the commencement of the murmur cannot be clearly dissociated. The murmur occupies the whole of diastole. (Fig. 3 and 6). In the remaining half a short gap occurs between second sound and murmur. The length of the murmur varies from  $\cdot 06$  to  $\cdot 25$  seconds, the average length being  $\cdot 16$  seconds. It begins from  $\cdot 06$  to  $\cdot 22$  seconds before *R*†; the average interval is approximately  $\cdot 14$  seconds. Where there is a gap between second sound and murmur it has usually been small, amounting to from  $\cdot 03$  to  $\cdot 07$  seconds (Fig. 5 and 7).

Thus we may conclude that in cases of mitral stenosis, where the heart beat is regular and, as is common, somewhat accelerated, the whole or greater part of diastole is usually filled by the murmur. It is noteworthy that in many of these cases the summit *P* falls back upon the preceding *T* or, what is equivalent, the whole of diastole is occupied by auricular systole.‡

The patients of whom I have so far spoken were unselected, except in so far as anything but regularity of action was concerned; they may be regarded as exemplifying the stage of the valve defect at which the working class patient usually seeks treatment.

I have specially selected two other patients in whom the signs were less conspicuous (Table III). In both of these cases the murmur was extremely short. In one, although the heart rate was accelerated, the murmur occupied only the last  $\cdot 07$  sec. of diastole. In the other the murmur was scarcely perceptible in the sitting posture, the posture adopted while the curves were taken. The apical and control curves are shown (Fig. 8 and 9); in the former the oscillations begin  $\cdot 05$  sec. earlier than those of the first sound in the control, commencing about a hundredth of a second before *R* and a few thousands of a second before *Q*.

---

\* The initial vibrations are often lost (1) because the murmur masks them and (2) because towards the base of the heart the breath sounds are often harsh and the breathing cannot as a rule be suspended in these cases for any length of time. The initial vibrations are also but poorly conducted to this region according to Fahr.

† The actual position may vary a good deal from cycle to cycle; the figures given are averages.

‡ Auricular systole begins, at the latest,  $\cdot 03$  sec. after the upstroke of *P*; it ends, when there is no heart-block, at the commencement of ventricular systole.



TABLE II.

|          | Curve.  | Rate. | Beginning of <i>Q</i> to 1st sound. | Beginning of <i>R</i> to 1st sound. | End of <i>T</i> to 2nd sound. | Length of 2nd sound. | End of 2nd to murmur. | Length of murmur. | Length of 1st sound. | Beginning of murmur to <i>R</i> . | <i>P-R</i> interval. | Vibration frequency. |            |         | Remarks.               |
|----------|---------|-------|-------------------------------------|-------------------------------------|-------------------------------|----------------------|-----------------------|-------------------|----------------------|-----------------------------------|----------------------|----------------------|------------|---------|------------------------|
|          |         |       |                                     |                                     |                               |                      |                       |                   |                      |                                   |                      | 1st sound.           | 2nd sound. | murmur. |                        |
| E. P.    | Apical  | 114   |                                     | 0.045                               |                               |                      | 0.03                  | 0.33              |                      | 0.14                              |                      | 54                   | 59         | 79      |                        |
|          | Control | 102   | No <i>Q</i>                         |                                     | 0.0                           | 0.07                 |                       | 0.19*             | 0.14                 |                                   | 0.17                 |                      |            |         |                        |
| L. H.    | A       | 140   |                                     |                                     |                               |                      | 0.04                  | 0.21              |                      | 0.06                              |                      |                      |            | 75      |                        |
|          | C       | 137   | 0.04                                | 0.03                                | -0.021                        | 0.07                 |                       | 0.09*             | 0.12                 |                                   | 0.14                 | 47                   | 54         |         |                        |
| J. V.    | A       | 109   |                                     |                                     |                               |                      |                       | 0.27              |                      | 0.12                              |                      | 70                   | 75         | 56      |                        |
|          | C       | 102   | No <i>Q</i>                         | 0.029                               | -0.011                        | ?                    |                       | 0.15*             | 0.12                 |                                   | 0.16                 |                      |            |         |                        |
| S. T.    | A       | 151   |                                     |                                     |                               |                      |                       | 0.38              |                      |                                   |                      | 55                   | 43         | 78      | Full diastolic murmur  |
|          | C       | 151   | 0.042                               | 0.035                               | 0.0                           | 0.08                 |                       | 0.13*             | 0.17                 | 0.09*                             | 0.15                 |                      |            |         |                        |
| L. W.    | A       | 119   |                                     |                                     |                               |                      | 0.05*                 | 0.22              |                      | 0.10                              |                      | 52                   |            | 48      | Second absent at apex  |
|          | C       | 120   | No <i>Q</i>                         | 0.020                               | -0.03                         | 0.09                 |                       | 0.13*             | 0.09                 |                                   | 0.22                 |                      |            |         |                        |
| J. H. H. | A       | 96    |                                     |                                     |                               |                      |                       | 0.47              |                      |                                   |                      | 60                   | 43         | 83      | Full diastolic murmur  |
|          | C       | 97    | 0.039                               | 0.026                               | -0.01                         | 0.10                 |                       | 0.25*             | 0.12                 | 0.22*                             | 0.19                 |                      |            |         |                        |
| M. W.    | A       | 96    |                                     |                                     |                               |                      | 0.07                  | 0.33              |                      | 0.17                              |                      | 64                   | 41         | 54      |                        |
|          | C       | 105   | 0.026                               | 0.019                               | -0.006                        | 0.10                 |                       | 0.19*             | 0.14                 |                                   | 0.16                 |                      |            |         |                        |
| C. S.    | A       | 108   |                                     |                                     |                               |                      |                       | 0.43              |                      |                                   |                      | 40                   | 39         | 41      | Full diastolic murmur. |
|          | C       | 111   | 0.047                               | 0.042                               | 0.003                         | 0.09                 |                       | 0.24*             | 0.10                 | 0.20*                             | 0.19                 |                      |            |         |                        |
| R. L.    | A       | 168   |                                     |                                     |                               |                      |                       | 0.26              |                      | 0.14*                             |                      | 67                   | 41         | 83      | Full diastolic murmur  |
|          | C       | 160   | No <i>Q</i>                         | 0.022                               | -0.003                        | 0.08                 |                       | 0.06*             | 0.12                 |                                   | 0.14                 |                      |            |         |                        |
| A. G.    | A       | 93    |                                     |                                     |                               |                      |                       | 0.38              |                      | ?                                 |                      | 50                   |            | 51      | Full diastolic murmur  |
|          | C       | 99    | 0.016                               | 0.006                               | -0.015                        | ?                    |                       | ?                 | 0.11                 |                                   | 0.22                 |                      |            |         |                        |

\* Calculated by subtraction.

TABLE III.

|       | Curve.            | Rate.      | Beginning<br>of <i>Q</i> to<br>1st sound. | Beginning<br>of <i>R</i> to<br>1st sound. | End of <i>T</i><br>to 2nd<br>sound. | Length of<br>2nd<br>sound. | End of 2nd<br>to<br>murmur. | Length of<br>murmur. | Length of<br>1st sound. | Beginning<br>of<br>murmur<br>to <i>R</i> . | <i>P-R</i><br>interval. | Vibration frequency. |             |              | Remarks. |
|-------|-------------------|------------|---|---|-------------------------------------|----------------------------|-----------------------------|----------------------|-------------------------|--|-------------------------|----------------------|-------------|--------------|----------|
|       |                   |            |   |   |                                     |                            |                             |                      |                         |  |                         | 1st<br>sound.        | 2nd<br>oun. | mur-<br>mur. |          |
| J. S. | Apical<br>Control | 154<br>133 | 0.03                                      | 0.02                                      | -0.005                              | 0.07                       | 0.03                        | 0.07*<br>0.17        | 0.10                    | 0.05                                       | 0.14                    | 100                  | 70          | 67           |          |
| H.    | A<br>C            | 78<br>82   | 0.035                                     | 0.028                                     | 0.007                               | 0.07                       | 0.28                        | 0.04*<br>0.18        | 0.14                    | 0.01                                       | 0.14                    | 67                   | 79          | 107          |          |

\* Calculated by subtraction.



Thus it appears that the shortest murmurs are confined to presystole, but that the longer ones stretch back further and further into diastole, filling it when the diastole is short, and either filling it, or more commonly just failing to fill it, when the diastole is longer.

The characters of these murmurs are variable, where they have the rushing quality to the ear, the vibrations are more frequent, where they are low pitched and rumbling, the frequency is less and approaches very nearly to the frequency of the first sound. In my records I see murmurs which increase in amplitude (Fig. 9), and others which decrease in amplitude as they progress (Fig. 7); the majority show little change (Fig. 3) or, increasing a little at first, they decrease subsequently (Fig. 6). Thus a conspicuous crescendo is present only exceptionally, and so infrequently that I think it evident that it is rarely formed by the murmur alone. The murmur oscillations are generally of smaller amplitude than those of the first sound; the crescendo which is audible is made up of murmur and first sound.

*The murmurs of mitral stenosis when auricular fibrillation is present.* Mitral stenosis is a condition in which the murmurs often change both in character and position; they change especially when the heart becomes irregular.

Mackenzie<sup>11</sup> was investigating a curious form of heart irregularity, which he had isolated and which is commonly associated with mitral stenosis. This irregularity he termed at a later date "nodal rhythm," largely because he could find no evidence of the auricular contraction in presystole; subsequent inquiry has proved it to be the result of auricular fibrillation. It should be clearly understood, therefore, that Mackenzie's original description applies to the changes in the murmurs when fibrillation (or what he terms "nodal rhythm") develops. Mackenzie's chief statement is that the presystolic murmur vanishes at the onset of the irregularity.\* Now while the general truth of this statement has received wide acceptance, yet a good deal of misconception has arisen, despite the repeated and detailed statements which have been made.<sup>14 & 15</sup> The difficulty has been, and still is, that a simple statement is insufficient. It is perfectly true that there may be a murmur in presystole while the auricle is fibrillating, but it is equally true that the murmur does not belong properly to presystole, though it may extend into it and even fill it. *The murmur is not found in presystole while the remaining portions of diastole are free from it.* My remarks are based upon the auscultatory phenomena in scores of patients and upon the phono-electrocardiograms in nine cases.

When the auricles fibrillate the ventricle beats rapidly and irregularly, and so the lengths of diastole are very variable. If the stenosis is of high grade and the heart beats sufficiently rapidly, then the murmur may fill diastole in each cycle (Fig. 10). But if a sufficiently long diastole occurs or if, as a result of treatment, the heart rate falls sufficiently, it becomes

---

\* Fagge, writing in 1871, stated that in a large proportion of cases of mitral stenosis in which no murmur was detected, the pulse was very rapid and irregular.

perfectly patent that the murmur has no fixed relation to the first sound, but that it has a fixed relation to the second sound.\* In the long diastole a gap appears between the murmur and the first sound. I publish a second curve (Fig. 11), taken from the same subject after treatment with digitalis; the heart rate has become much slower, but it remains irregular. During the shortest diastole in this photograph the relations of the murmur are precisely the same as those seen in Fig. 10. But in the remaining diastoles the murmur tails away and the curve is unbroken by oscillations for a variable period until the pause ( $p$ ) is terminated by the abrupt onset of the succeeding first heart sound. When the heart rate is lower still, the beats are often in couples, constituting the now well recognised digitalis bigeminy (Fig. 12, from the same case). After the second beat of each couple the diastole is of unusual length, and it is occupied by a diminuendo murmur commencing in early diastole. The heart is silent during the periods immediately preceding the first sound; it is in such hearts that it may be said without qualification, there is no presystolic murmur. The same relations of the murmur are to be seen in the phono-electrocardiograms of my other patients and I show another example in Fig. 13. The control curve is shown in Fig. 14.

There are several features of this early diastolic murmur which are of diagnostic importance, helping to distinguish it from the early diastolic murmur of aortic disease.† It has the same relatively slow frequency of vibration as have the other murmurs of mitral stenosis. The murmurs of aortic disease are generally of higher pitch. A short though appreciable interval is often apparent between the murmur of mitral stenosis and the preceding second sound; this is seen at  $x$  in Fig. 11 and 13. When the interval is large or when diastole is short, its presence brings the murmur into the position of mid-diastole. The explanation of the interval will be discussed again.

*The murmurs of mitral stenosis when heart-block is present.* It has been stated by Mackenzie<sup>16</sup> that when the *As-Vs* interval is prolonged, so that there is a distinct intersystolic gap, the position of the murmur which commonly falls in presystole alters, and that it becomes more mid-diastolic in time; that is to say, there is an interval of silence between murmur and first sound. The same conclusion was arrived at from less perfect data by Galabin. His curves of auricular and ventricular contraction were taken from the apex beat. Cohn<sup>3</sup> has reported an instance of heart-block, in which at the appearance of 2:1 heart-block, he heard two murmurs during each diastole. Personally, I have made many observations of the same sort and they all tend to support the view that the positions of the diastolic

---

\* Galabin,<sup>10</sup> in 1875, recorded cases of mitral stenosis in which there was a diastolic murmur only, and stated that in these he could find no trace of auricular contraction in curves taken from the apex beat.

† The common view that aortic regurgitant murmurs may be heard only at the apex beat requires reconsideration. It is a view for which these early murmurs of mitral stenosis are probably largely responsible; they are often mistaken for aortic murmurs.



murmurs of mitral stenosis are largely controlled by the positions of the auricular systoles. Thus when dropped beats are present in mitral stenosis, the thrills and murmurs occur at irregular intervals, sometimes seeming to precede the apex thrust, at other times lying in early or mid-diastole or disappearing altogether. It is well-nigh impossible to accurately time either thrills or murmurs in relation to the several phases of diastole when the ventricle beats irregularly; and it is in such cases that simultaneous electrocardiograms and heart sound records should be of especial value.

At the present time I can describe only a single case of the kind. When this patient first came under observation the *P-R* interval measured .22 sec., and there was a murmur of .13 sec. duration in presystole (Fig. 15). The control curve is shown in Fig. 16. Under digitalis heart-block developed and two mechanisms were exhibited.

In one the heart action was regular but the auricle, instead of contracting in presystole, contracted earlier and simultaneously with the ventricle (Fig. 17), the *P-R* interval being .36 seconds. The accompanying sounds were curious. The first and second sounds were heard, and also a brief sound or murmur lying apparently in mid-diastole. The sound record (Fig. 17) shows a large first sound, a small second sound and a short murmur in mid-diastole. The presystolic part of the cycle is silent.

In the other the heart was irregular and the curves obtained were extremely complex (Fig. 18). We may conveniently describe this curve by numbering the ventricular cycles. The first sound is seen in each cycle, but it varies in amplitude; in cycles 1 and 3 it is of small amplitude and both the corresponding ventricular contractions are directly preceded by auricular contractions; in cycles 2, 4 and 5, the first sound is of greater amplitude, and here the auricular and ventricular contractions are simultaneous; the variation in amplitude is ascribed to the varying relation of the ventricular to the auricular systole (see Griffith<sup>12</sup>). In Fig. 17 where the two systoles are always synchronous, the amplitude is great and of constant amount. The second sounds of Fig. 18 are all small, but are easily distinguished because they occupy a constant relation to the first sounds. The time relations of the murmurs are very variable. A presystolic murmur appears on two occasions, namely, directly before the first sound of cycles 1 and 3. These murmurs correspond to the auricular contractions  $P^1$  and  $P^4$ . There are early diastolic murmurs of considerable amplitude and of the diminuendo type in cycles 1, 3 and 4; these correspond to the auricular contractions  $P^2$ ,  $P^5$  and  $P^6$ . In cycles 3 and 5 this murmur is absent and the auricular contractions  $P^3$  and  $P^7$  fall very far back into the ventricular systole. I have described a single curve, but similar events are seen in a number of other curves from the same case. There seems to be a definite relation between the position of murmur and auricular systole.\*

---

\* The single inconsistency is in the after events of  $P^3$  and  $P^6$ .  $P^3$  is followed by a second sound and a trace of murmur;  $P^6$  by a second sound and a loud early diastolic murmur. The inconsistency is a small one and possibly resulted from respiratory interference.

*The causation of the diastolic murmurs in mitral stenosis.*

The presystolic murmur, described by Fauvel<sup>8</sup> in 1843, and attributed by him to auricular systole, has been the subject of much discussion. I do not propose relating the arguments which have been brought forward in support or in condemnation of this view. The discussion has turned chiefly upon the timing of the murmur, some believing it to be truly presystolic,\* others regarding it as really systolic.†

The only accurate method of determining its time relations is the graphic one, and this shows its diastolic position quite clearly. In considering its cause we can concern ourselves only with diastolic events, and must attribute it to the onflow of blood through a constricted mitral orifice. We may clearly understand the origin of the diastolic murmurs of mitral stenosis when we have a true conception of differential pressures in left auricle and left ventricle, for the velocity of the blood flow will depend upon the difference between the two pressures. The difference in pressure is never great in the normal heart during diastole, for the orifice joining the chambers is a wide one. But it is greatest at two periods of diastole; when the auriculo-ventricular valves open and during the systole of the auricle. In mitral stenosis the differential pressures are almost certainly greater and especially so towards the end of diastole if the auricular walls are hypertrophied.

The diastolic murmurs of mitral stenosis appear at the points when they are anticipated, if we hold this view of their causation. When the heart is slow, when there is a normal sequence of chamber contraction and a slight or moderate grade of stenosis, we find a presystolic murmur alone; if the stenosis is greater, an early diastolic murmur may be added; the period of silence between the two murmurs corresponds to the period when filling is at its slowest.‡

In extreme stenosis the whole diastolic period may be full. Increased heart rate will also tend to produce full diastolic murmurs, for diastole is curtailed and the blood must enter the ventricle more speedily if the same quantity is to be maintained in circulation. Anything which increases the output of the heart, such as exercise or the increase of venous filling, the latter accompanying the recumbent posture, must have a similar effect; and the same influence will unmask a murmur which is audible only on occasion.

The alterations in the murmurs at the onset of heart irregularities teach us a great deal. That the *isolated* presystolic murmur is related to auricular systole seems clear, for it is not present when the auricles are fibrillating, neither is it present when, as a result of heart-block, the auricular contraction occupies an unusual position in the cardiac cycle. That the auricular contraction is responsible for murmurs seems apparent too from a further

\* Gairdner<sup>9</sup> first termed it the auriculo-systolic murmur.

† Full reference to the original papers will be found in Brockbank's book.<sup>1</sup>

‡ It seems quite possible that if in a long diastole the ventricle becomes engorged, the differential pressure at the contraction of the auricle may be insufficient to produce a presystolic bruit.



consideration of these instances of heart-block ; the position of the murmur alters according to the position of the auricular systole : more observations of a graphic nature are certainly required in this connection, but the records from the solitary case already described are peculiarly significant.

In auricular fibrillation the site of election for the appearance of a murmur is early diastole and not presystole ; the murmur may fill diastole when the rate is fast or when single diastoles are short, but in the longer diastoles, be they solitary or in succession, the murmur finishes before the first sound. The murmur does not always begin at the termination of the second sound, and this for an obvious reason : the semilunar valves close before the auriculo-ventricular valves open. The interval between the two valve movements is greatest when the heart beats slowly, and it is under these conditions that the gap between second sound and the commencing murmur is often heard.

To sum up, the evidence in our possession leads us to believe that the diastolic murmurs of mitral stenosis are produced by the rush of blood from auricle to ventricle, and that the position of the murmur in diastole is controlled by the velocity of the blood flow. The murmurs first appear at those portions of diastole at which the differential pressure is greatest. When the normal sequence is maintained, one of these portions is presystole, and the velocity is greatest at this time because the auricle is in contraction. That the murmurs should have a strict time relation to auricular systole is hardly to be expected under all circumstances, for the pressures may be affected in many ways ; but that very definite time-relations are often established is clear from the graphic records of irregular heart action.

### CONCLUSIONS.

1. The relation of the normal first sound at the apex to the initial ventricular deflection of the electrocardiogram in lead *II* is variable. It may commence within .011 sec. of *Q* or .002 sec. of *R* ; or it may be delayed until .026 sec. after *R* or .039 sec. after *Q*. Usually it begins a little before or after the summit of *R*.
2. The relation of the normal second heart sound at the apex to the end of *T* is variable. It may commence .01 or even .03 sec. before this point, but more usually it starts at the end of *T* or .01 or .02 sec. afterwards.
3. The relations of the first and second sounds near the apex, to the deflections of the electrocardiogram in mitral stenosis, are practically the same as in normal hearts. The duration is also very similar to the normal.
4. The shortest murmurs of mitral stenosis precede the first sound and consequently precede the initial rise of intraventricular pressure. They lie in presystole.

5. Generally speaking the presystolic or diastolic murmur is not a crescendo ; the crescendo is an effect of the proximity of the loud first sound. The vibration frequency is from 41 to 107 per second ; usually the frequency is low (average 68·5). The murmur begins from ·05 to ·22 sec. before the commencement of *R* and runs up to the first sound.

6. When fibrillation of the auricles is present, an isolated presystolic murmur does not occur. The fixed relation of the murmur is to the early phases of diastole.,

7. When heart-block is present the positions of the murmurs are largely controlled by the positions of the auricular contractions.

8. The diastolic murmurs of mitral stenosis are due to the rapid onflow of blood through the stenosed orifice. Those periods of diastole are occupied by murmur, during which the velocity reaches a certain grade. When the auricle contracts at the normal time and the heart beats slowly the velocity tends to be greatest in presystole, otherwise it is greatest in early diastole ; these are the times at which murmurs are most commonly audible.

#### BIBLIOGRAPHY.

- <sup>1</sup> BROCKBANK. "The Murmurs of mitral Disease." Edin. and Lond., 1899.
- <sup>2</sup> BULL. Quart. Journ. of exper. Physiol. 1911, IV, 289.
- <sup>3</sup> COHN. Brit. med. Journ., 1909, II, 1153.
- <sup>4</sup> EINTHOVEN. Archiv. f. d. ges. Physiol., 1907, CXVII, 461.
- <sup>5</sup> EINTHOVEN. *Ibid*, 1907, CXX, 31.
- <sup>6</sup> FAGGE. Guy's Hosp. Rep., 1871, 3rd Ser., XVI, 247.
- <sup>7</sup> FAHR. Heart, 1912-13, IV, 147.
- <sup>8</sup> FAUVEL. Archiv. gén. d. méd., 1843, I, 1.
- <sup>9</sup> GAIRDNER. Edin. med. Journ., 1861-2, VII, 438.
- <sup>10</sup> GALABIN. Guy's Hosp. Rep., 1875, 3rd Ser., XX, 282.
- <sup>11</sup> GIBSON. Lancet, 1907, II, 1380.
- <sup>12</sup> GRIFFITH. Heart, 1911-12, III, 143.
- <sup>13</sup> KAHN. Archiv. f. d. ges. Physiol., 1909, CXXVI, 197 ; 1910, CXXXII, 209 ; 1910, CXXXIII, 597.
- <sup>14</sup> MACKENZIE. "The Study of the Pulse." Edin. and Lond., 1903.
- <sup>15</sup> MACKENZIE. Brit. med. Journ., 1904, I, 529 ; 1905, I, 759 ; Quart. Journ. of Med., 1907-8, I, 39 ; "Diseases of the Heart," Lond. 1908, 297.
- <sup>16</sup> MACKENZIE. Amer. Journ. med. Sci., 1907, CXXXIV, 12 ; "Diseases of the Heart," Lond., 1908, 171 and 325.
- <sup>17</sup> WEISS AND JOACHIM. Archiv. f. d. ges. Physiol., 1908, CXXIII, 341. (See also Gerhartz, "Die Registrierung des Herzschesalles," Berl., 1911.)



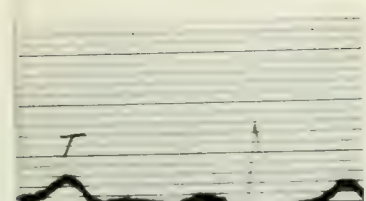


Fig. 1.  
the  
of  
of  
ver  
elec  
10

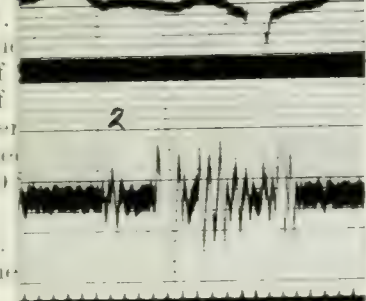


Fig. 2.  
the

Fig. 3.  
tak  
mur  
sou  
fille  
The  
figu  
the  
in t

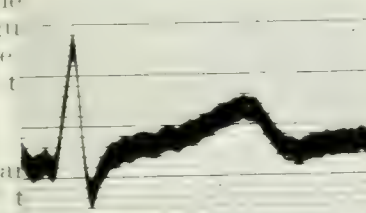


Fig. 4.  
hear  
At t  
coul  
Fig.

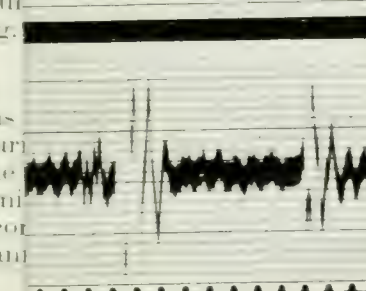


Fig. 5.  
was  
mur  
The  
dimi  
seco  
man

Fig. 6.  
the a  
and  
diast  
first  
of the

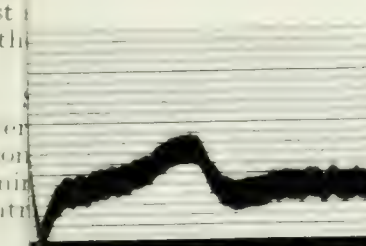


Fig. 7.  
exter  
seco  
dimin  
contr

Fig. 8. S  
epiga

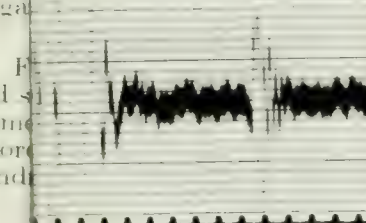


Fig. 9. P  
and s  
seem  
reco  
hund

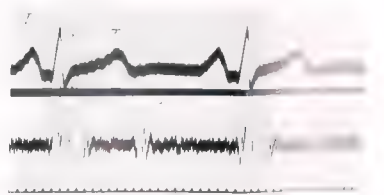
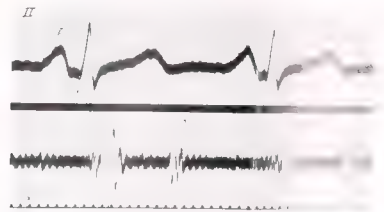
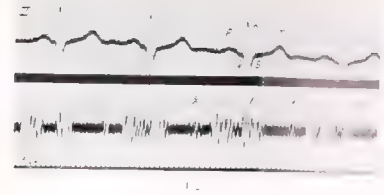
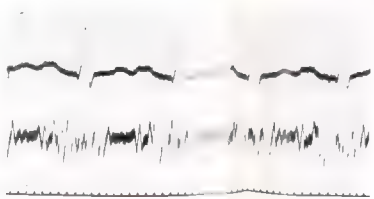
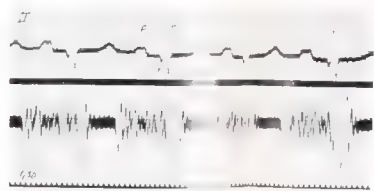
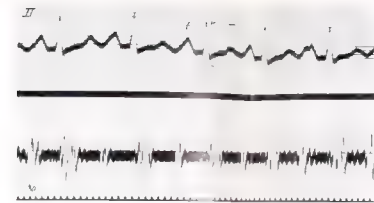
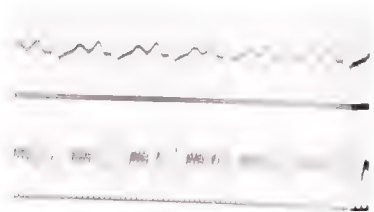
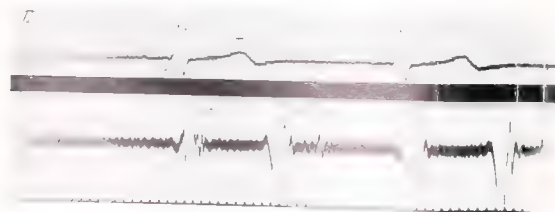
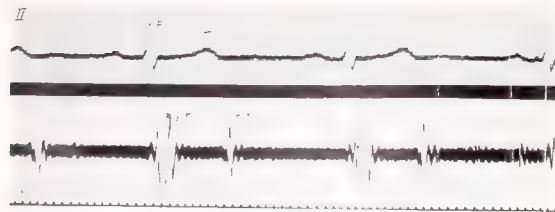


Fig. 8.



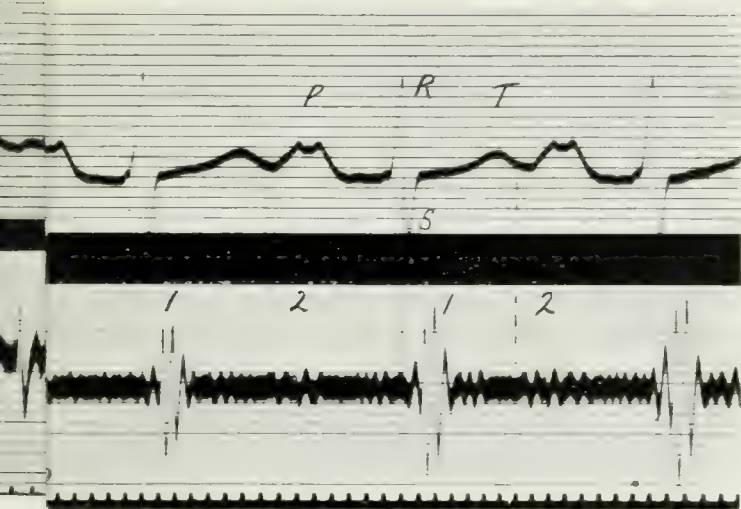


Fig. 16.

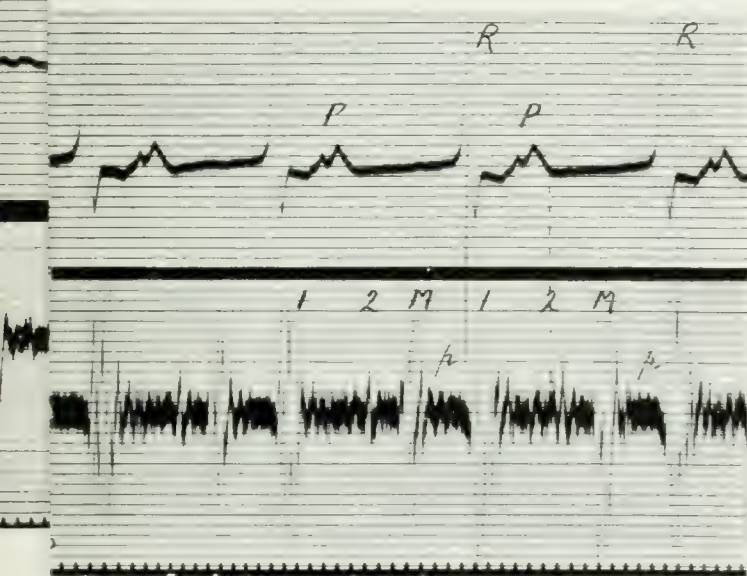


Fig. 17.

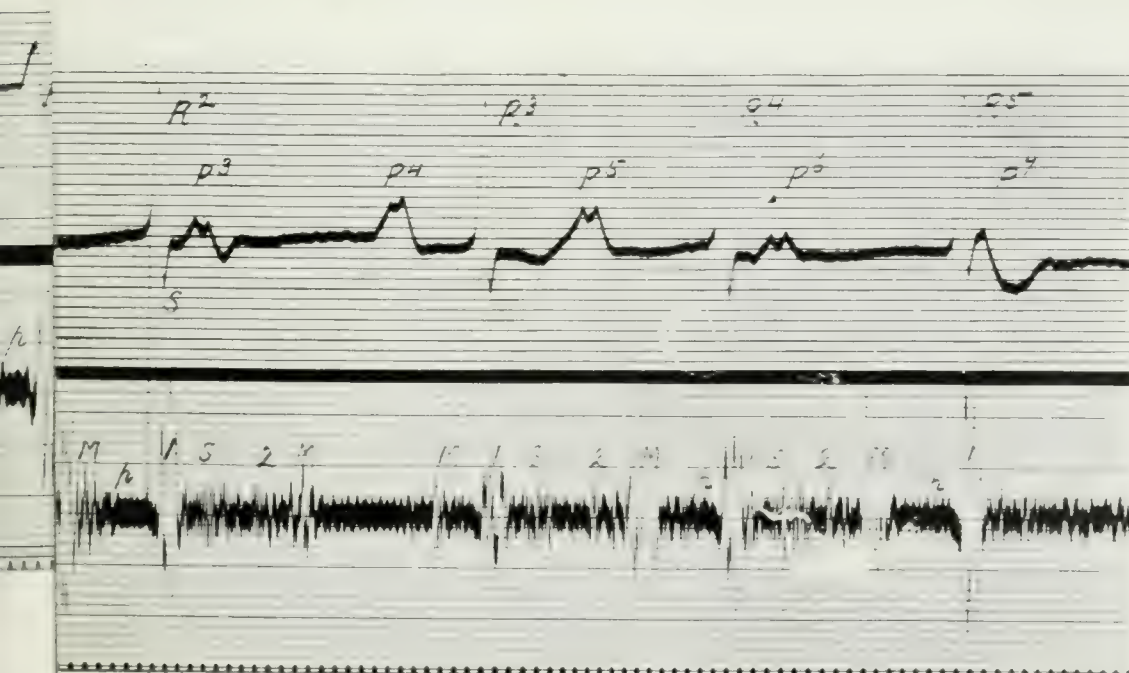
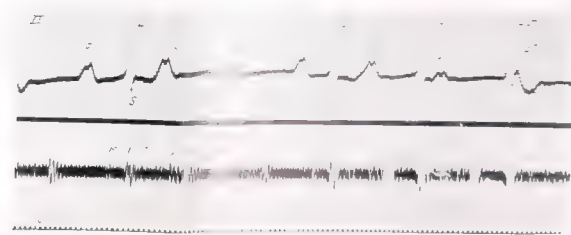
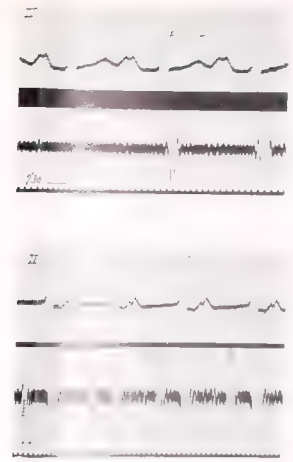
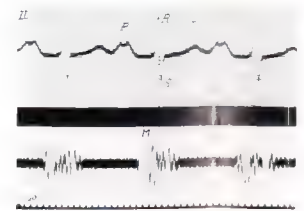
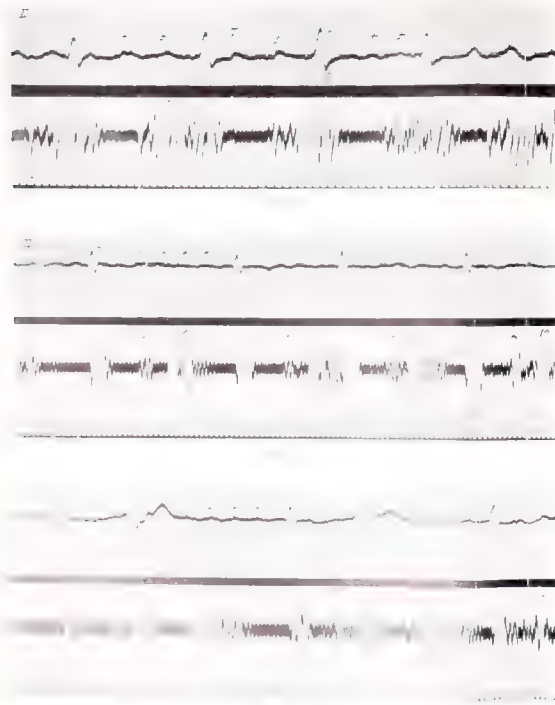


Fig. 18





## SOME PROPERTIES OF SURVIVING ARTERIES.

By J. ELRICK KESSON, M.D.

*Lecturer on Experimental Physiology in the University of Aberdeen.*

*(From the Physiological Laboratory).*

### I.—REACTION OF ARTERIES TO INTERNAL PRESSURE.

SOME years ago Bayliss<sup>1</sup> described some remarkable facts in connection with the reaction of blood vessels to alterations in internal pressure. He found from plethysmographic experiments that after section of the vascular nerves of a limb or organ the blood vessels responded to a rise of internal pressure by increased contraction and to a fall of pressure by relaxation. He emphasised the importance of this peripheral power of reaction—which occurred also with intact nerves—in providing as far as possible for the maintenance of a constant flow of blood through the tissues, limbs, brain, &c., supplied by them whatever may be the height of the general blood pressure, except in so far as they are directly over-ruled by impulses from the central nervous system. An important part is ascribed to the same mechanism in cases where as great as possible a rise or fall of the arterial pressure is required. Hill and Flack<sup>7</sup> have applied these results in the comparison of the arterial pressures in the arm and leg and in the two arms when one is held up and the other down. They assume inequality of contraction in the arteries in these cases on the ground that an artery exposed to increased pressure (due to hydrostatic effect in this instance) contracts while one exposed to lessened pressure relaxes.

Again, Hill<sup>6</sup> affirms that the arteries contract by themselves to increased pressure, while the vaso-motor system controls the arterioles.

Bayliss's conclusion as to the automatic response of arteries to changed internal pressure is corroborated by Bier's<sup>2</sup> observation that in a pig's leg disconnected from the animal's body, except the connection afforded by an arterial cannula, active hyperæmia followed temporary arrest of the arterial flow, the reaction being evidently independent of the central nervous system.

Starling<sup>11</sup> states that after severance of the nervous connections increased tension acts as a stimulus to increased contraction and cites the response of a strip of carotid (even a day or two after death) to a sudden distending force by a slow contraction.

Inquiring into the nature of the vascular reaction in question Bayliss performed a few experiments on excised arteries and though he did not follow up this line of investigation he pointed out the importance of a positive

result, which he obtained notably in one asphyxiated dog's artery two hours after death, as showing that the arterial reaction to changes of internal pressure is not due to any other cause than the change of tension, and that it is myogenic in character.

*Methods of experiment.*

While experimenting on arteries for various purposes I have very frequently examined the effects of rises and falls of internal pressure in over 170 arteries taken from more than ninety animals (horse, ox, dog, cat, &c.). The carotids, femorals, metatarsals, and metacarpals were chiefly used. The vessels were often taken immediately after death and tested in a few minutes; in other cases at varying periods up to some hours after death, being kept in the meantime in cold Ringer's solution or blood from the same animal, defibrinated or treated with hirudin. The lengths of artery to be tested were tied on a cannula and placed in a glass plethysmograph connected with a tambour or with a horizontal tube of small bore fitted with a millimetre scale to indicate displacement of fluid depending on volume changes in the artery. The artery was filled and surrounded in the plethysmograph with blood or Ringer's solution, oxygenated or shaken up with a mixture of oxygen and carbon dioxide (5 per cent). Yandell Henderson<sup>13</sup> has described the important part played by a normal CO<sub>2</sub> content in the blood in maintaining the tone of the unstriped muscle of the intestine.

The plethysmograph and its contents were kept at about body temperature by immersion in a suitable water bath or jacket.

Some of the arteries were taken from anæsthetised animals killed in different ways, but most from horses and oxen slaughtered in the usual way; a few from cats, rabbits, &c., killed by shooting, &c.

The pressure within the artery was raised by elevation of the reservoir supplying the fluid or of a mercury bottle which displaced fluid from the reservoir, or by successive strokes of a pump—to imitate as far as possible the nature of a rise of pressure in the normal circulation.

The condition of the artery as regards the absence or presence in varying degree of tonic contraction may possibly be of much importance in connection with the reaction now being considered. There is evidence available from various sources bearing on the essential relation between a certain degree of tonus and a certain degree of distending pressure in the production of a rhythmical response, though the precise relation between the degree of tonus and the internal pressure effective in inducing rhythmical contractions has not been defined. Such evidence is to be found in the work of Sokoloff and Luchsinger,<sup>10</sup> Jastreboff,<sup>8</sup> Elliott and Barclay-Smith,<sup>5</sup> Cannon,<sup>3 & 4</sup> and others, derived from a study of the ureter, vagina, bladder, œsophagus, colon, &c. It is known that the amount of tonus present may be relatively too great or too small. In view of the uncertainty on this point and the absence of any knowledge as to possible relations with a contractile reaction in the arteries it is obviously important to test the vessels in very different conditions



as regards the absence and degree of tonus. Short pieces of artery (carotid of ox, &c.), in the plethysmograph often show decided persistent contraction even when kept at  $38^{\circ}$  C. in Ringer's fluid or blood, possibly on account of the mechanical stimulation of cutting, ligature, &c., at the ends. Longer portions (10 to 15 cm.) were often used and were found to present varying grades of tonus—in some practically none, as evidenced by the trivial amount of external pressure necessary to obliterate the tube, by the character of the expansion increments rising to a maximum when tested by successive rises of internal pressures, &c.; in other cases varying grades of tonus, up to strong persistent contraction were in evidence.

In Bayliss's very striking experiments on denervated limbs and organs the rise and fall of pressure often lasted 10-40 seconds; then when the pressure returned to the normal the contraction or relaxation (responsive to the original rise or fall) appeared and lasted for at least as long afterwards, often much longer. There was then a return to the normal, directly or after "reverberation." The rises and falls of pressure in his experiments seem to have been pretty extensive as a rule, though varying considerably, *e.g.*, rises of 70 mm. from a level of 110, of 50 from about 120, and of 35-40 from about 65, and falls of 40 from 110, 40 from a pressure of 70. In one tracing a marked reaction is seen in the plethysmogram to follow so small a rise of blood pressure as 14 mm. The duration of the reaction in relation to the duration of the change in pressure responsible for it is worthy of note. Sometimes a fall lasting about ten seconds gives a subsequent expansion of the limb lasting about forty seconds; a fall of twenty seconds was followed by expansion for thirty seconds. The expansion induced by a fall often lasted twice as long as the fall.

Thus the relaxed artery evidently failed for a considerable time to respond to the stimulating influence of the renewed inrush of blood and increase of pressure. Similarly a rise of pressure causes contraction which does not for a considerable time yield to the relaxing influence of the lowering of pressure down to the original level.

In the present inquiry the amount and duration of the changes of internal pressure have been made to vary within wide limits. As regards amount, such alterations as these were induced—rise to 120, lowered to 80; rise to 160, lowered to 70; rise to 200, lowered to 60; rise to 180, lowered to 90; rise to 180, lowered to 60; rise to 160, lowered to 90; rise to 140, lowered to 80.

The pressure was commonly raised quickly as shown in the tracings—more quickly than would occur in the circulation—but in some instances a slower rate of increase was adopted. The fall was similarly varied.

The changed levels of pressure were maintained for periods varying from a few seconds to many minutes. In some cases a slight or moderate pressure, *e.g.*, 60 mm., &c., was got up and steadily maintained for prolonged periods. In other cases the pressure was raised by 20 or 40 mm. at a time and kept at each level for a definite period; then lowered to zero to test the recovery

*Results.*

Under all these different variations the behaviour of the arteries examined was notably constant as regards the essential feature of showing no active response either in the direction of contraction against a rise or relaxation against a fall of internal pressure ; the arteries practically behaved like passive tubes expanding with a rise and diminishing in volume with a fall of pressure. When an artery has been distended by a high pressure it may after the pressure has fallen to zero become and remain for long periods of somewhat smaller volume than before indicating a slight increase of tone in the vessel. This is in accordance with what was noted by MacWilliam<sup>9</sup> many years ago ; it does not bear out the view that there is contraction against increased and relaxation towards diminished pressure. Even after high pressures and marked distension the artery shows very evident signs of vitality, contracting markedly on stimulation (cutting, &c.).

The general nature of the results is illustrated by the tracings here reproduced. Fig. 1 calls for no comment except that at the end of the

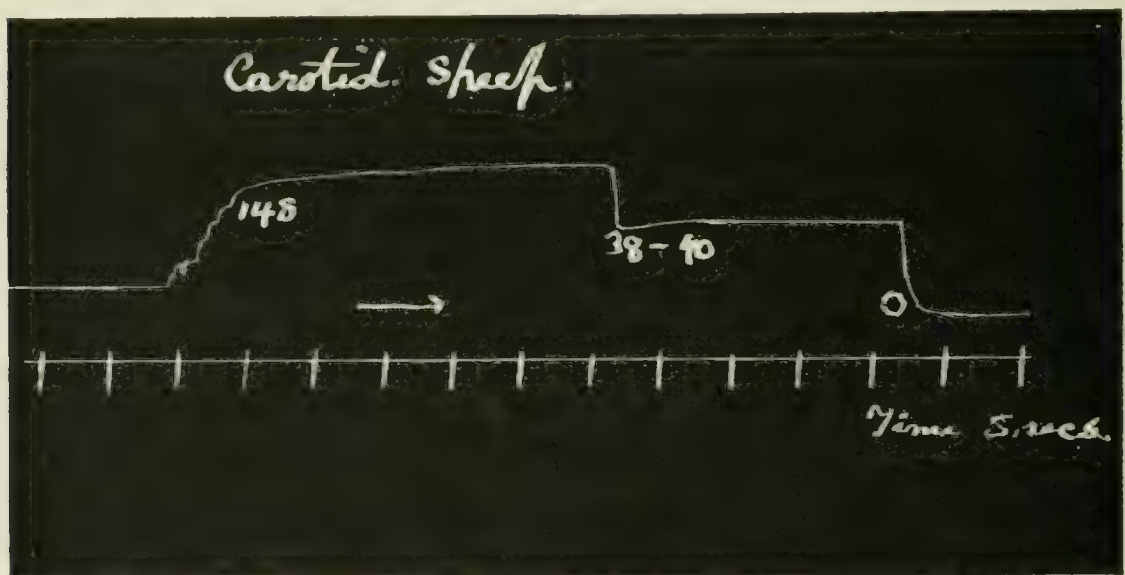


Fig. 1.

tracing the volume of the artery is somewhat smaller than before ; it remained persistently so after the pressure had been down to zero for many minutes. The oscillations on the rise are due to the movements of the pump used to raise the pressure. The close relation between increase of pressure and increase of volume and *vice versa* are well seen in Fig. 2, obtained from another sheep's carotid with a recording tambour which magnified much more ; the rise of pressure to 100 mm. lasted about forty seconds. At the end of the tracing the volume is still somewhat larger than to begin with ; the slow recovery of the artery is not yet completed. Two carotids from different oxen tested with considerable pressures gave the results seen in Fig. 3 and 4. The pressure of 200 mm. in Fig. 4 was maintained for about



thirty seconds. Fig. 5 shows two rises of pressure in an ox carotid. Continued gradual expansion occurs while the high pressure lasts. Between and after the rises the volume does not diminish to the normal as sufficient time was not allowed for the slow completion of the recovery of the stretched arterial wall,—this did not occur till much later. As the arteries of the horse retain their responsiveness to stimulation specially long, I have made a considerable

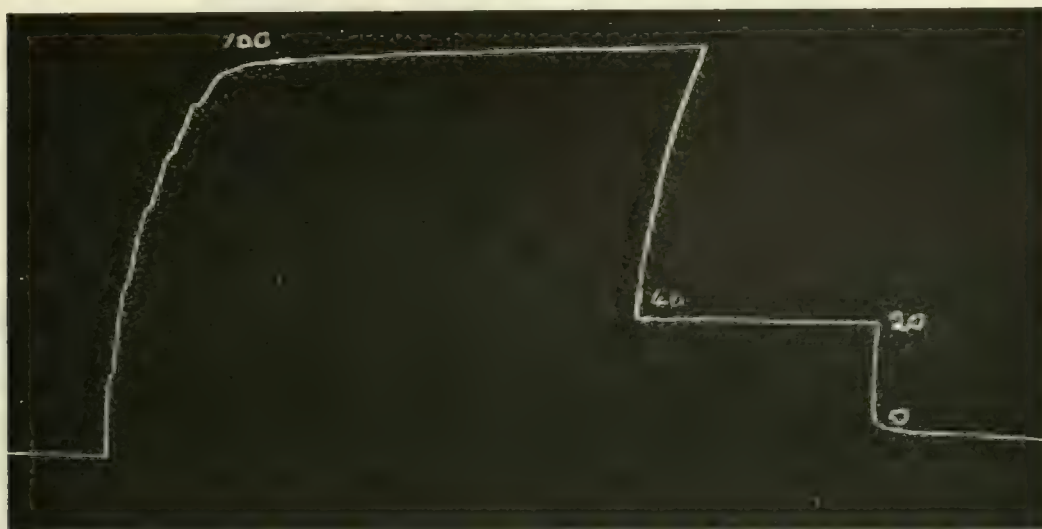


Fig. 2.

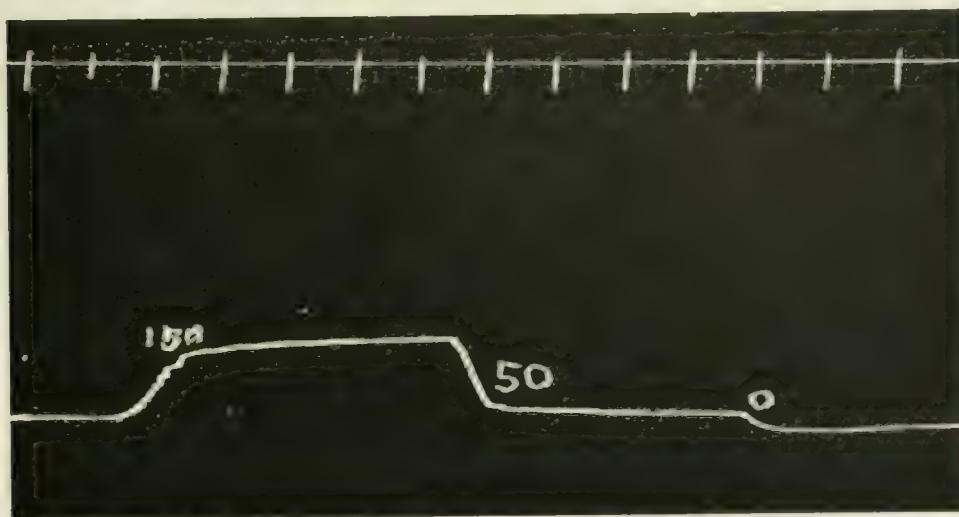


Fig. 3.

number of observations upon them, using the carotids, metacarpals, metatarsals, &c. The latter with their powerful muscular coats are well adapted for the study of reactions to internal pressures. In some cases I have tested these arteries at the slaughter house a few minutes after the animal was struck down, and in all cases with negative results as far as active reactions are concerned. Fig. 6 is from a carotid, and Fig. 7 and 8 from

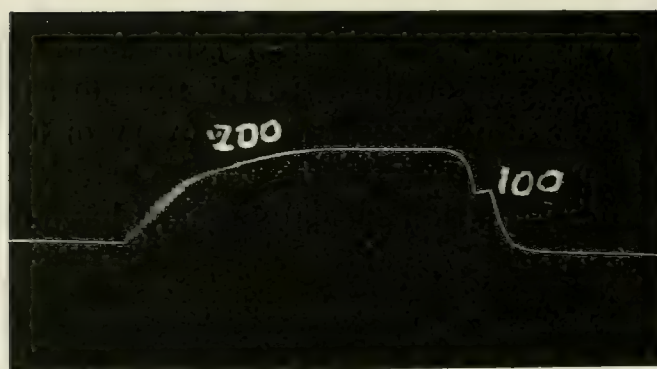


Fig. 4.

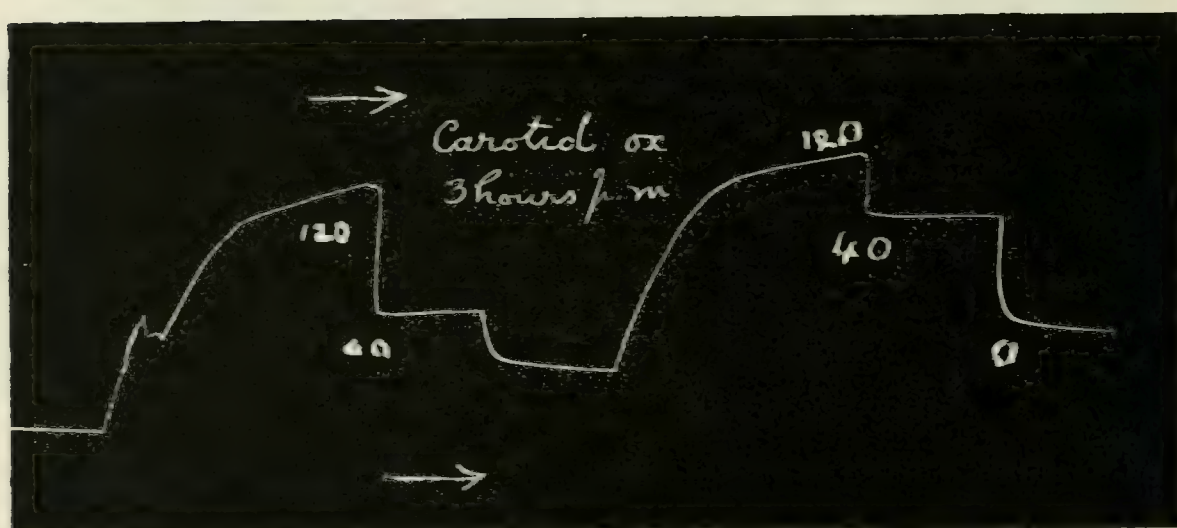


Fig. 5.

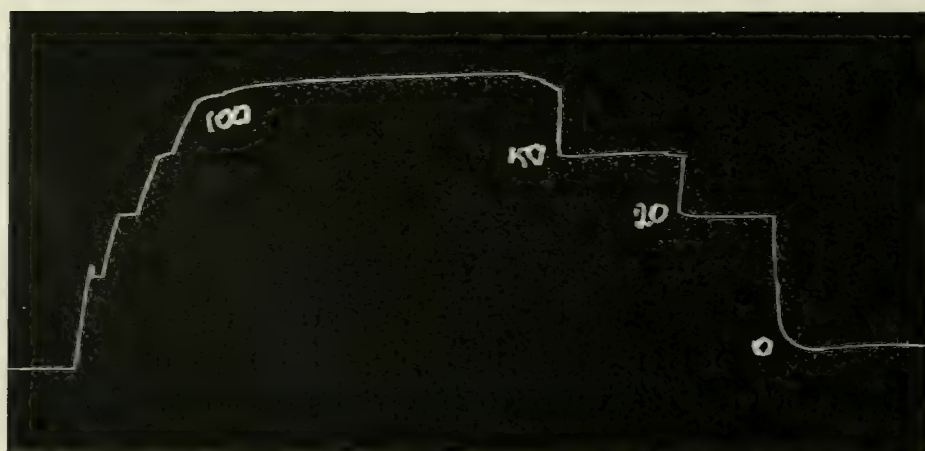


Fig. 6.



metacarpals. The close correspondence between the volume and pressure changes in the vessel behaving as a passive elastic tube are very evident. The slowness of expansion often seen in these arteries (contracted) is to be noted in Fig. 8. Marked rhythmical contraction is also sometimes seen under pressure.

In none of my experiments was any active reaction to altered internal pressure recognisable by the eye in cases where a plethysmographic record was not taken. I have indeed on rare occasions noticed visible contraction of an artery after tying up upon the cannula, &c.; but this seemed to be clearly attributable to mechanical stimulation. Had this occurrence

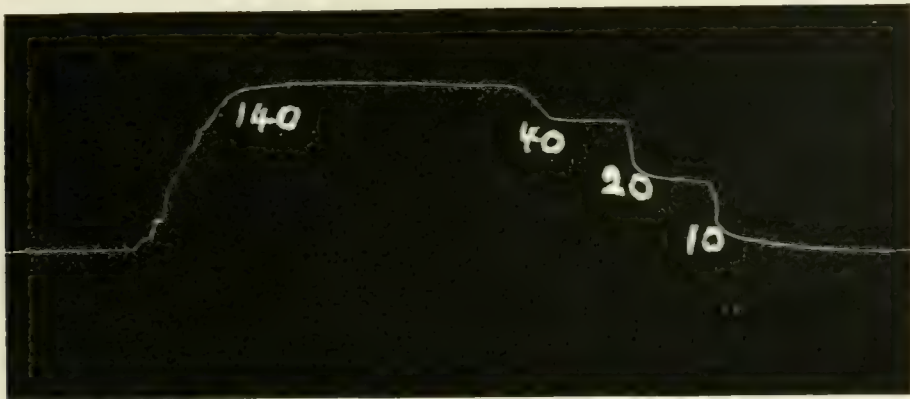


Fig. 7.

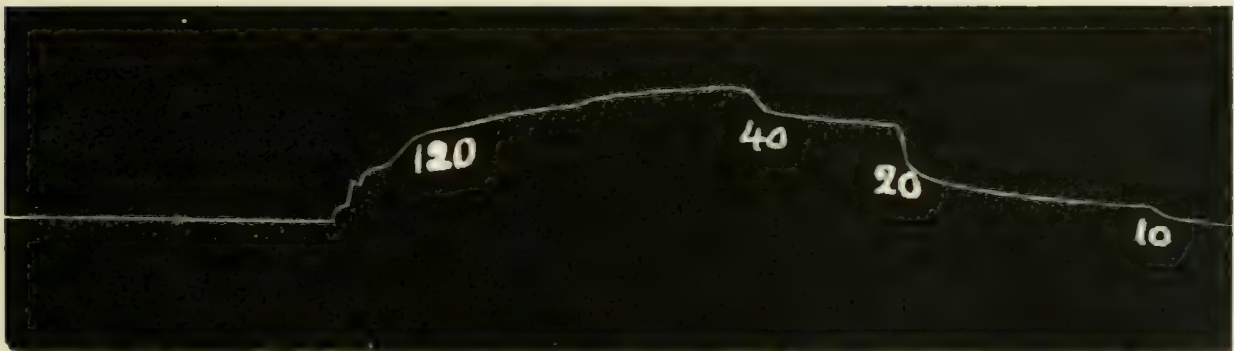


Fig. 8.

coincided with the artificial production of a rise of internal pressure it might easily have been ascribed to the influence of the latter.

*Resistance to obliterating pressure at different perfusion pressures.* Another method of testing the alleged occurrence of increased contraction in response to increased tension and *vice versa* is to determine the value of the resistance which the arterial wall offers to obliterative pressure when perfused with fluid at very different internal pressures. If the arterial muscle reacts by contraction and relaxation to raised and lowered internal pressure, such ought to be evidenced by changes in the resistance to compression offered

by the arterial wall. Using large arteries like the carotid of the ox with its powerful muscular coat it is easy to observe the variations in resistance to compression depending on the presence of varying amounts of contraction. The results obtained in this way strongly oppose the hypothesis that increased contraction is excited by increased tension and *vice versa*. With great alterations of internal pressure the resistance of the arterial wall is not appreciably changed, showing that there is no important change in the way of contraction or relaxation, *e.g.*, in the case of a carotid (ox) tested in the usual way at body temperature a few hours after excision at internal pressures of 22, 28, 86, 122, 118 mm., in another at internal pressures of 36 and 78, and in a third at internal pressures varying from 18-128 mm. The obliteration pressure was estimated in some instances almost immediately after the change in internal pressure was made, in other instances after the altered internal pressure had been acting for some minutes.

#### *Discussion of results.*

Hill and Flack<sup>7</sup> conclude that increased contraction or rigidity in arteries leads to a higher systolic reading in blood-pressure estimation by the obliteration method; this they attribute to better conductance of the systolic wave in more contracted or more rigid arteries. Hill and Flack made observations on the upper limbs when one arm was held up and the other down so as to give very considerable differences in pressure from hydrostatic causes; they made similar observations on the arm and leg where the differences in pressure were extensive. From other observations, those investigators conclude that increased contraction or rigidity in an artery influences the systolic reading in an important way by better conductance of the systolic wave. Now if the arteries react to increased pressure by increased contraction and *vice versa*, and increased contraction alters the systolic reading it is clear that the readings in the foregoing observations should differ more than would be accounted for by the hydrostatic factor.

But this is not what has been found to obtain; Hill and Flack found that the pressure in the upraised and lowered arms and in the arm and leg differ from one another only by the amount of the hydrostatic pressure; hence the existence of appreciable differences in contraction—even in the presence of great differences in internal pressure—is negatived. Here the evidence opposes the hypothesis of a reaction of the artery to altered internal pressure—assuming the correctness of the view that changes in the amount of contraction express themselves by modification of the systolic readings—through altered conductance or other causes. Hill and Flack believe that the effects of greater contraction or greater rigidity in the arterial wall are so potent as to account for the striking disparity (100 mm. or more) between the systolic readings from the arm and leg readings in cases of aortic regurgitation and in healthy young men after severe muscular exertion such as stair-climbing. Bier's observation of hyperæmia in a limb being induced by a temporary anæmia even after severance of the connection with the



central nervous system has already been cited ; it obviously fits in well with the conception of a local independent reactive power in the arteries. But that the matter is not always susceptible of so simple an explanation is shown by Bier's experiment of stopping for a time the blood-supply to two loops of intestine, one of them empty and the other containing milk at body temperature. When the blood stream was readmitted the empty loop showed no hyperæmia while the milk-filled one became actively hyperæmic ; he also found that the intestine of a fed animal becomes hyperæmic after a similar re-establishment of the circulation, while that of a fasting animal does not. According to the same observer the dog's stomach gives hyperæmia in similar circumstances and the rabbit's stomach does not. In view of such results it is evident that the hyperæmic reaction following temporary anæmia is by no means always or necessarily a simple reaction of the arterial muscle—relaxation or expansion induced by decreased tension, but depends in some cases at least on the working of a more complex mechanism.

It is important to bear in mind that an automatic regulation of the size of the arteries by a simple response to increased or diminished pressure within them would involve not only a contraction answering to an increased stretch or pull (as is said to occur in the bladder, the body of the earthworm, &c.) but a continued contraction persisting as long as the rise of pressure lasts, and relaxation equalling in duration the lowering of pressure inducing it.

There seems to be no available evidence of the existence of such a reaction in unstriated muscle excluded from possible nervous influences. In hollow viscera like the stomach and bladder with a sheet of unstriated muscle in their walls, receptive relaxation—instead of responsive contraction occurs when fluid is gradually introduced. In the case of the stomach Cannon and Lieb<sup>4</sup> find that this relaxation is mediated through the vagus nerve.

The contractile response which may occur in a strip of carotid when suddenly stretched is too crude an experiment to be valid evidence in this connection. The traction is applied to the muscular elements of the arterial wall in an abnormal way and the pull is excessively sudden and violent as compared with what is exercised by such changes of pressure as may occur in the circulation. The same probably holds good with the responses in the body wall of the earthworm, &c. In skeletal muscle it is well known that a sudden tug or strain on the tendon may cause contraction, but such requires to be sharp and of considerable force. The most rapid extension of a muscle in the execution of a normal movement does not stimulate the muscle.

It is, of course, a familiar fact that in hollow viscera, &c. (bladder, stomach, intestine) internal tension may in favourable circumstances as regards tone, &c., lead to the development of a rhythmic series of single contractions (as I have also noted on some occasions in the metacarpal artery of the horse) but this is quite a different phenomenon of a strong and persistent contractile response to raised internal pressure.

## II.—EFFECTS OF COLD, EXPOSURE TO AIR AND MECHANICAL STIMULATION ON ARTERIES.

It is commonly accepted that arteries are made to contract by cold and exposure to air, and the hard contracted state of viscera containing unstriated muscle (*e.g.*, uterus, stomach, &c.), is usually ascribed to the same causation. Contraction of unstriated muscle (from this cause) near the neck of the bladder has been regarded as possibly an important factor in post mortem experiments on the urine-retaining mechanism.<sup>12</sup>

The writer's experiments on surviving arteries, &c., under various conditions has led him to the conclusion that the above-mentioned view is incorrect. He finds that cold and exposure to air apart from mechanical disturbance do not cause contraction, but that when contraction has been induced by mechanical irritation or other form of stimulation (electrical, &c.) cold has an important and remarkable effect in rendering the contraction persistent for long periods (days).

Observations have been made on the head and neck of the sheep, the horses' leg, amputated human limbs, the carotids of the horse and ox excised while still enclosed by a considerable amount of surrounding tissue, &c. After the parts had been at ordinary room temperature or cooled down to a few degrees above 0° C. for hours or for a day or two the arteries when carefully exposed were found to be still uncontracted and flattened in shape, often even after the necessary precautions had been taken to obviate the possibility of flattening of the tube being due to (1) tension between its attachments, or (2) an obstacle to the entrance of air necessary to allow the tube to become rounded if there was a tendency for such to occur.

When the covering tissues were carefully removed with a minimum of mechanical disturbance, using perfectly clean instruments, the arteries remain without visible sign of contraction for many hours though freely exposed to the air, precautions being taken to prevent drying, &c., by enclosing the parts in a moist chamber.

Later, mechanical stimulation by cutting and gentle manipulation, caused striking contraction, the tube becoming circular and firm with a greatly diminished lumen (one-half, one-third, &c.). Thus a horse's carotid twenty-four hours post mortem changed its diameter from 6 mm., its size in relaxed state, to 3 mm. Very striking results of a similar nature were seen in the horse's metacarpal. After a portion of the leg had been kept in a cold chamber for three or four days with the artery partially exposed to the air the vessel was still soft and flattened; when dissected out and cut the lumen narrowed till only a fine bristle could be inserted. This contraction persists for many hours or for days at room temperature or at some degrees above 0° C. On warming to body temperature the artery relaxes more or less completely, there being considerable variation as to the extent of this relaxation.

The behaviour of unstriated muscle in these respects is strikingly different from what we are familiar with in ordinary striped muscle.



## III.—INFLUENCE OF TEMPERATURE ON ARTERIAL ELASTICITY.

In 1902 MacWilliam described the long persistence of vitality in excised arteries and certain fundamental differences in the distensibility of contracted arteries on the one hand and that of relaxed arteries and of veins on the other; these differences were associated with characteristic features in the extensibility of strips cut from the various kinds of vessels. In the present inquiry attention was directed to the influence of temperature on these changes.

The arteries employed were the carotid of the horse, sheep and dog, the femoral of the cat, and the metacarpal, hepatic, &c., of the horse. After

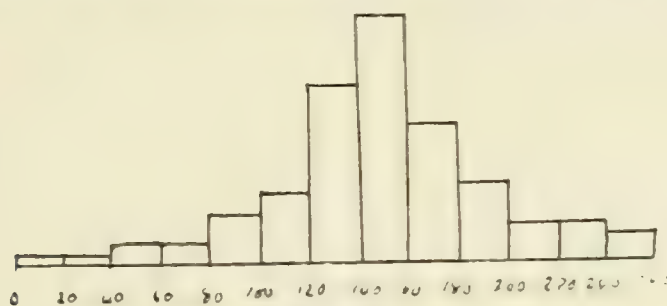


Fig. 9.

excision shortly after death they were placed in defibrinated blood or oxygenated Ringer-Locke fluid; if not used immediately they were kept in a cooled chamber. When being tested the arteries were kept at body temperature by suitable baths,\* &c.

The results show conclusively that at body temperature the behaviour of the vessels is essentially similar to what occurs at room temperature. The maximum distensibility of contracted arteries varies with the amount

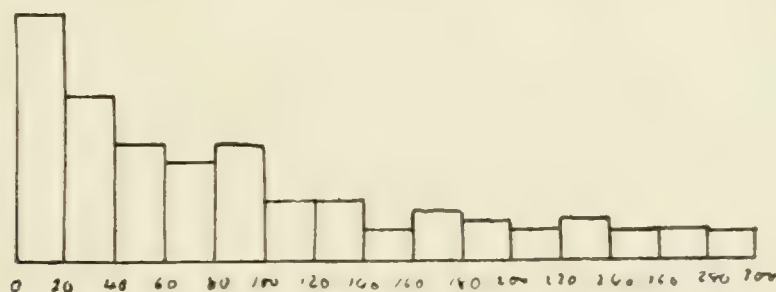


Fig. 10.

of contraction present, and may occur at very different internal pressures, *e.g.*, at 140 to 160 as shown in Fig. 9, or at 0 to 20 as in Fig. 10. Both these are from the carotid of the ox distended by 20 mm. increments of internal pressure each lasting one minute. Arteries strongly contracted at room temperature are more or less largely relaxed by warming to 37° or 38° C., and according to the amount of contraction persisting the position of the maximum increase of volume early or late in the series. When there is

\* The methods are described elsewhere. (This paper, page 260.)

complete relaxation the maximum increase of cubic capacity per unit increase of internal pressure comes at the beginning of the series as is seen in Fig. 10, thus resembling what occurs in a non-muscular artery or a vein.

Strips of the arterial tube when extended by weights behaved as at room temperature, allowing for the varying amounts of contraction which may be present when warm.

In strongly contracted thickened arteries (*e.g.*, some metacarpals of old horses) very high distending pressures may be required; no appreciable effect is produced up to a certain point, the artery behaving almost like a rigid tube, and this in the absence of calcareous or markedly fibrous changes, the thickening being essentially a muscular hypertrophy.

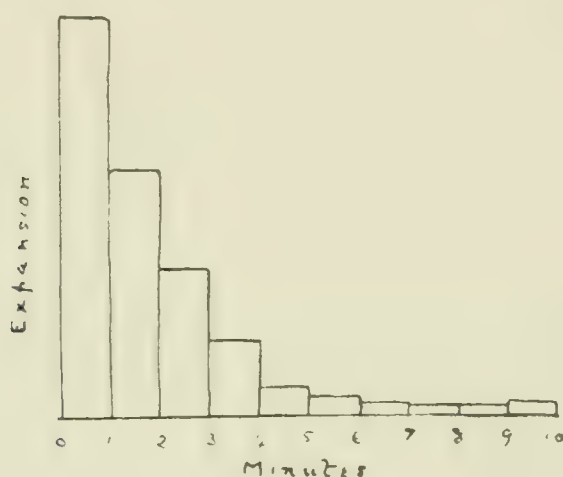


Fig. 11.

The time relations of the distension by internal pressure in contracted and relaxed arteries respectively, are worthy of note. Under a pressure sufficient to cause marked expansion the contracted vessel yields slowly, the increase of volume in the second and third minutes taken together often being quite as large as that of the first minute; the total increase in ten minutes may be about  $2\frac{1}{2}$  times the expansion of the first minute as is shown in Fig. 11.

The relaxed artery on the other hand, tested with similar pressure, yields quickly so that the expansion is nearly completed in the first minute; the subsequent increase is so slight that at the end of ten minutes the total volume may be only one-twentieth more than at the end of the first minute.

#### SUMMARY

Excised surviving arteries—large or medium sized—examined plethysmographically behave like passive elastic tubes when subjected to extensive rises and falls of internal pressure; they show no sign of reacting by contraction against an increased or by relaxing against a lowered pressure.



The resistance of the arterial wall to obliterative pressure shows no marked or constant difference with great alterations of internal pressure: this is against the hypothesis of responsive changes in the way of contraction and relaxation of the arterial muscle.

The observation that in the human body limb arteries with very different internal pressures (due to hydrostatic influence) give identical blood pressure readings when the hydrostatic factor is allowed for indicates that no appreciable reactive change is present in the arterial walls in response to the different internal pressures.

While Bier's observations on a limb show hyperæmic reaction to temporary anæmia apart from the influence of the vaso-motor centre, his results on the intestine and stomach must be interpreted as indicating that the hyperæmic reaction is not always or necessarily a simple reaction of the arterial muscle to altered tension.

The volume changes in denervated limbs and certain organs recorded by Bayliss show important reactions in some portion of the vascular circuit of the limb or organ, but do not indicate which part is concerned.

The results of the present inquiry are opposed to the hypothesis that altered internal pressure causes this reaction, at least so far as arteries of large or moderate size are concerned: they show no evidence in support of the hypothesis of a myogenic origin of such reaction.

The occurrence of such a reaction in the arterioles while absent in the medium-sized and large vessels would imply a notable physiological difference in the musculature of different parts of the arterial tube.

As regards their elastic properties, whether tested by distension under internal pressure or by the loading of strips cut from their walls, surviving arteries show at body temperature the same characteristic differences between the contracted and the relaxed states found at room temperature by MacWilliam, the contracted giving increments of volume or length progressively rising to a maximum and then diminishing, while the relaxed show the maximum effect at the beginning of a descending series.

The expansion of a contracted artery under a rise of internal pressure is very gradual and slow in developing as compared with a relaxed artery, and the recovery when the pressure is lowered shows a notable difference.

Cold, *per se*, does not cause contraction of arteries, though it greatly influences the persistence of contraction excited by other causes.

NOTE.—Since this paper was written Von Anrep has published (Journ. of Physiol., 1912, XLV, 318) evidence to show that Bayliss's results on denervated limbs and organs are to be ascribed to other causes than altered tension—the increased contraction to the influence of adrenalin, the relaxation to the action of asphyxial products on the vessel wall. With excised arteries Von Anrep obtained negative results; he does not publish any tracings. He concludes that local reaction of the vessel wall to changes of tension is as yet unproven.

## BIBLIOGRAPHY.

- <sup>1</sup> BAYLISS. Journ. of Physiol., 1902, xxviii, 220.
- <sup>2</sup> BIER. "Hyperæmie als Heilmittel," Leipzig, 1903.
- <sup>3</sup> CANNON. Amer. Journ. Physiol., 1911-12, xxix, 238.
- <sup>4</sup> CANNON AND LIEB. Amer. Journ. Physiol., 1911-12, xxix, 267.
- <sup>5</sup> ELLIOTT AND BARCLAY-SMITH. Journ. of Physiol., 1904, xxxi, 289.
- <sup>6</sup> HILL. "Further Advances in Physiology," London, 1909, 126.
- <sup>7</sup> HILL, FLACK AND HOLTZMANN. Heart, 1909-10, i, 74.
- <sup>8</sup> JASTREBOFF. Archiv. f. Physiol., Phys. Abth., 1884, 103.
- <sup>9</sup> MACWILLIAM. Proc. Roy. Soc., 1902 lxx, 109.
- <sup>10</sup> SOKOLOFF AND LUCHSINGER. Arch. f. d. ges. Physiol., 1881, xxvi, 467
- <sup>11</sup> STARLING. "Textbook of Physiol.," London, 1912, 1113.
- <sup>12</sup> STARLING. Schäfer's Textbook of Physiol., London, 1898, ii, 341.
- <sup>13</sup> YANDELL HENDERSON. Amer. Journ. Physiol., 1909, xxiv, 70.



## AN OBSERVATION RELATING TO THE NATURE OF AURICULAR FIBRILLATION.

By THOMAS LEWIS.\*

*(Cardiographic Department, University College Hospital Medical School).*

THERE are many questions relating to fibrillation of the auricles and ventricles to which no final answers can be returned at the present time. Fibrillation of a muscle mass is still but imperfectly understood and any account which pretends to explain the nature of the condition can only be regarded as a working hypothesis.

In writing of the condition known as fibrillation of the auricles I have repeatedly advocated the view that it results from the formation of new impulses in the muscle at a number of abnormal and ectopic foci. One of the most striking features of auricular fibrillation is the nature of the ventricular response. Fibrillation is never transmitted as such from auricle to ventricle, but the ventricle beats in a co-ordinate though perfectly irregular fashion. The responses are the result, as Fredericq<sup>2</sup> has shown, of impulses traversing the auriculo-ventricular bundle; they are impulses escaping in haphazard fashion from the quivering auricle. I have pointed out that similarly when the ventricle fibrillates the auricle responds irregularly to it,<sup>2</sup> an observation which has also been recorded by Cohn and Mason.<sup>1</sup> The auriculo-ventricular bundle, while conducting the impulses of a fibrillating auricle or ventricle, does so in a peculiar fashion. It evidently does not conduct all such impulses, but sifts them.

I may illustrate my working conception of a fibrillating auricle or a fibrillating ventricle and the events related thereto by a simple illustration. Imagine, in the course of a smooth and narrow stream, a sudden expansion (Fig. 1). A pool through which water flows to find exit in a narrow and confined channel. If a succession of waves is propagated on the surface of the water at the side of the pond remote from the outlet, they will travel over the pond. Each wave will spread over the surface of the water as an arc of an enlarging circle and eventually will meet the bank at all points. It will also spread to the outlet and will advance along it with its ends touching the banks and its general line at right angles to the course of the stream. Moreover, if the waves are propagated regularly at their starting point, they will travel along the outlet regularly. Such I imagine to be the analogous conditions in a regularly contracting heart, where the pool represents the auricle and the outlet the A-V bundle.

---

\* Aided by a grant from the British Medical Association.

But suppose the water in the same pool to be disturbed at a large number of separate points (Fig. 2), so that the whole surface is lashed into innumerable waves and ripples, travelling in many directions. What happens at the outlet? If this be sufficiently narrow the separate outgoing waves will be of the same form as before; the general line of each will be at right angles to the stream, and after the immediate outlet is passed they will no longer clash but will pursue each other in parallel course along the length of the stream. Nevertheless their succession will be a perfectly irregular one. Such I imagine to be the analogous conditions when the auricle is fibrillating.

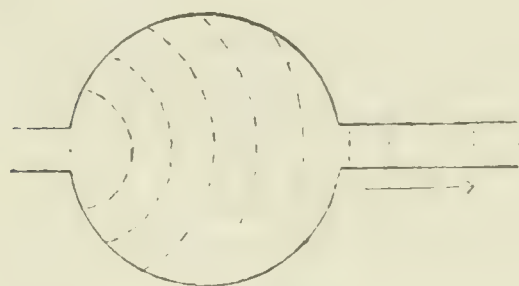


Fig. 1.

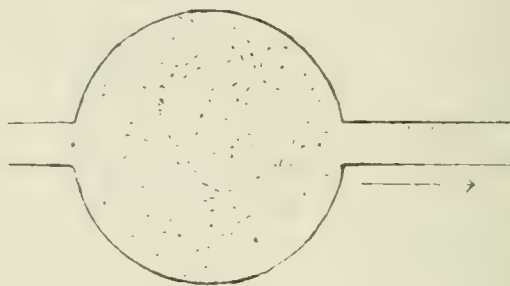


Fig. 2.

Fig. 1 and 2. Diagrams, illustrating the writer's conception of the paths taken by the contraction waves in the auricle. 1, while the auricle beats co-ordinately and 2, while it fibrillates.

The hypothesis has suggested a simple experiment. If it be correct, then the reason why the *A-V* bundle fails to convey fibrillation from one chamber to another is that it is a narrow channel.

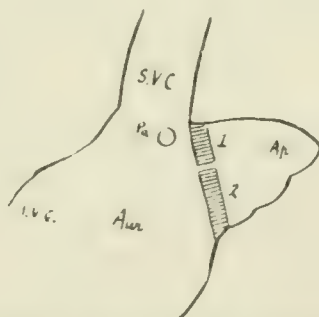


Fig. 3. A diagram of the right auricle, showing the positions (1 and 2) in which the clamp is applied to the base of the appendix. *Pa*—pacemaker.

For the purpose of the corroborative experiment, I have used dogs, anæsthetised with morphia, paraldehyde and ether. The heart is exposed and a fine suture run under the epicardium at the tip of the auricular appendix. Stretching the appendix, a strong clamp is applied across its base (Fig. 1), at such pressure as to break the softer muscular tissue without destroying the stronger epicardium and endocardium; the success of the crush is indicated by the transparency of the tissues directly after the clamp is removed. The crush is carried half across the appendicular base (1), starting



from the cavo-appendicular angle, and the clamp removed. The appendix regains its former outline and contains its blood. A second crush (2) is carried up towards the first from the *A-V* groove, so that the two almost meet. The muscle of the auricular appendix is thus isolated from that of the main mass of auricular tissue, except at two points, one in front and one behind. By twisting the appendix a little and reapplying the clamp, one of the bridges is easily broken without damage to the remaining one. The appendix is now in connection with the auricle by a single muscle bridge which can be reduced in size if it is desired.

The rest of the experiment consists in faradisation of appendix and auricle and observing the effects electrocardiographically. *When the auricle is faradised*, the usual fibrillation of auricle results and the ventricle beats quite irregularly in response to it. The fibrillation of the auricle is recognised by the disappearance of the *P* summits from the electrocardiograms and by the appearance of irregular oscillations (*f.f.* Fig. 5 and 6). It is difficult to state what happens to the appendix meanwhile, as its movements are confused by the irregular tug from auricle and ventricle.

*If the appendix is faradised* with the same current it is seen to fibrillate, but the auricle does not fibrillate, it beats rapidly, co-ordinately and irregularly. The relation of appendix and auricle which exists when the bridge of tissue is sufficiently narrow is precisely that of auricle and ventricle under ordinary circumstances. A fibrillating auricle produces co-ordinate but grossly irregular ventricular contractions. A fibrillating appendix produces co-ordinate but grossly irregular auricular contractions and the auricular disturbance is accompanied by a parallel, or almost parallel, ventricular action (Fig. 4, 7 and 8).

In the electrocardiograms the ventricular action is irregular but each ventricular beat is preceded by an auricular one. A gross irregularity, in which auricle and ventricle participate is seen.

Thus it is shown that the hindrance to the passage of fibrillation itself from auricle to ventricle or from ventricle to auricle is not necessarily the result of peculiar properties of the junctional tissues, but is more probably due to the simple narrowness of the tract along which the impulses course.

It is necessary that the bridge between appendix and auricle should be reduced to a millimetre or a little less before the desired result is obtained; the final stages in the reduction may be accomplished by means of a sharp and pointed knife. Complete destruction of the bridge immediately precludes the passage of any impulses which, if they traversed the bridge, would produce irregular action of the auricle.\* If, under these conditions, the appendix is faradised, it fibrillates, while the auricle continues its regular beating.

The type of electrocardiogram obtained after crushing the base of the appendix and faradisation of the appendix is not without interest. The

---

\* Fredericq has recently reported a similar observation (*Archiv. internat. de Physiol.*, 1912, xii, 109).

bridge lies in the immediate neighbourhood of the pacemaker (*Pa*). It sends forth impulses and these originate contraction waves which course through the auricle in an almost normal direction. The auricular representative in the curve, which is distinct before each ventricular contraction, is of very similar form to that of the normal beat in the same animal (Fig. 7, 8 and 9).

There remains but a single consideration. If the appendix is faradised before its base is crushed, the whole auricle fibrillates; after the crushing, fibrillation is confined to the appendix. The fibrillation which results in the main mass of the auricle when, as in these experiments, a faradic current is applied by means of a bi-polar electrode to the appendix, is not due to simple spread of the current to the auricle; if that were so the main mass of auricle should fibrillate subsequent to the crushing. Fibrillation spreads through living tissue. The fibrillation of a muscle area distal to stimulation results from the state of surrounding tissue elements. As a bridge, having a sectional area of one square millimetre is sufficient to transmit fibrillation as such, it seems probable that fibrillation is induced in a given mass of tissue if an area of *fibrillating* muscle of these dimensions is in continuity with it. In this may be found the reason why fibrillation, when once established, tends to persist, for unless it is brought to a close in all parts of the auricle or ventricle simultaneously, the area in which it persists should maintain the condition in all adjoining areas.

#### BIBLIOGRAPHY.

- <sup>1</sup> COHN AND MASON. Heart, 1911-12, 111, 341.
- <sup>2</sup> FREDERICQ. Archiv. internat. de Physiol., 1904-5, 11, 281.
- <sup>3</sup> LEWIS. Quart. Journ. of Med., 1909-10, 111, 337.









# THE ESTIMATION OF SYSTOLIC BLOOD-PRESSURE IN MAN WITH SPECIAL REFERENCE TO THE INFLUENCE OF THE ARTERIAL WALL.

BY J. A. MACWILLIAM AND J. E. KESSON.

(*From the Physiological Laboratory of the University of  
Aberdeen*).

THE first part of this paper deals with an experimental investigation of the properties of surviving arteries as bearing on the estimation of the pressure inside them, and the second part with the application of the experimental results to clinical conditions.

## PART I.

### *Previous investigations.*

Von Basch,<sup>18</sup> testing the radial arteries by a somewhat crude method, found that only 1 mm. Hg. was required to close healthy vessels and not much more than 5 mm. for sclerosed vessels.

C. J. Martin<sup>8</sup> worked with the carotids of man, horse and dog, perfusing them with a non-pulsatile stream of water and testing the external pressure necessary to stop the flow. In healthy arteries he found 2 mm. sufficient, and not more than 7 mm. in an advanced case of sclerosis. He concluded that a determination of the external pressure necessary to obliterate an artery is a valid indication of the internal pressure with the small deductions just stated.

Hill<sup>4</sup> concludes that the obliteration method is exact, and does not admit that resistance of the arterial wall to compression has any appreciable effect on the readings. He and Flack<sup>5</sup> measured the difference in two arteries placed at different levels in relation to the heart, the proof being that the pressure differs by the hydrostatic pressure of the column of blood between the two points of measurement. They reason that this would be very unlikely to hold good if the arterial wall affects the reading, as different arteries vary in pathological cases, and also from the improbability of the two arteries being equally contracted in view of their being exposed to different pressures, it being assumed that an artery exposed to lessened pressure dilates, while to increased pressure it contracts. (This last assumption, however, has been invalidated by recent work.) As another means of verifying the accuracy of the systolic index the same observers measured the venous pressure in the forearm while an armlet compressing the brachial artery was kept at 5 mm. Hg. below the obliteration pressure; they found

that the venous pressure rose to the pressure present in the brachial armlet, thus showing the obliteration method to be correct, at least within 5 mm. They obtained a result within 20 mm. in a case with hard arteries and an obliteration pressure of 220 mm. in some later observations.

Mummery,<sup>10</sup> repeating experimental observations by Riva-Rocci and Gumprecht compared the obliteration pressure as estimated by an armlet on the thighs of three dogs with the intra-arterial pressure recorded by a mercury manometer at the same time and found confirmation of the accuracy of the obliteration method. It may be noted that the pressures found are abnormally low for the dog's femoral (64-110 mm.) as compared with the usual values, suggesting that possibly the tone of the arterial wall may have been very slight. An ordinary manometer was used; without a valve it is impossible to measure systolic pressure with any accuracy with a mercury manometer.

Hensen<sup>2</sup> advanced evidence throwing doubt on the sclerosed arterial wall markedly affecting the readings.

Russell<sup>12</sup> has repeatedly urged the importance of hypertonus in sclerosed arteries, and has depicted very thick-walled vessels (radials, &c.) showing much thickening of the muscular coat, the hypermyotrophy of Savill. He contends that arterial hypertonus, rather than arterial hypertension, is largely what is measured by the obliteration method. He regards the changes in high readings following the administration of vaso-dilating drugs, &c., as due to the effect of the latter on the wall of the brachial artery rather than on the actual blood-pressure inside the artery; the evidence he lays most stress on in support of this view is derived from palpation of the arterial tube (radial usually). But he adduces no evidence to exclude change in the peripheral arterioles under the influence of these drugs as the dominant factor in determining a lower reading, depending on a lowering of the actual blood pressure. Russell has experimented with rubber tubes and with arteries which had been treated with formalin. The significance of such experiments is however greatly impaired by their remoteness from the conditions present in living arteries. Rubber tubes are known to offer great resistance to obliteration, as do arteries after formalin, but the relation of the behaviour of such tubes to that of living arteries is a remote one.

Russell argues that a small thick-walled tube must offer more resistance to compression than a larger thinner-walled tube. While this is unquestionably true, *caeteris paribus*, it does not carry us far towards any definite idea of the importance of the arterial wall in blood-pressure estimations. For as the resistance of the relaxed brachial artery is merely nominal (one or two millimetres of mercury), it is obvious that if the resistance in the contracted state were several times greater it would still be of little moment. How much more resistance is offered by the wall of a contracted artery cannot be deduced from a comparison of the relative measurements. It is clear that the resistance offered by the contracted muscle can only be determined by direct experiment under conditions of precision in living arteries.



Oliver<sup>11</sup> ascribes considerable importance to the resistance of the arterial wall on the ground of the decided differences which he has sometimes found between the two arms and between arm and forearm by the armlet method; also on account of the different readings which he has obtained by his hæmadynamometer as compared with the armlet method, especially in pathological conditions and in old age. In regard to the latter Hill expresses doubts as to the reliability of the hæmadynamometer readings.

Muller and Blauel<sup>9</sup> making observations during amputations found the obliteration pressure to be 7 to 10 mm. above the true systolic pressure.

Volhard<sup>17</sup> obtained some rather higher values, 10 to 13 mm.

Herringham,<sup>3</sup> perfusing *post-mortem* arteries with a non-pulsatile stream of water, found considerable differences in the obliterating pressure, 4-22 mm., and in one a resistance of 34 mm. Hg. He reported similar findings in eight arteries (one of 60 mm.) after means had been taken to exclude the possible existence of persistent contraction. The existence of some torsion in the artery has been suggested by Janeway and Park as possible cause of resistance in these cases.

Williamson,<sup>19 & 20</sup> examining high-pressure cases with degenerated arteries has found differences between the arm and leg pressures in the horizontal position sometimes amounting to 50 mm. Hg.

Scholtyssek<sup>16</sup> and Schmidt<sup>15</sup> using excised arteries recorded varying resistances of no great amount.

Janeway and Park<sup>7</sup> experimented with dead human vessels (carotids, iliacs and vessels from amputated limbs) and also with surviving arteries from oxen (presumably healthy animals), chiefly carotids, but including a few mesenterics. From these experiments they conclude that atheroma has no appreciable effect on the compressibility, and calcification only a moderate effect, and that in clinical determinations under suitable conditions even advanced arterial thickening and calcification probably do not introduce an error of any importance. Contraction of the arterial muscle they find to be a definite factor in influencing compressibility; they regard as improbable any error of more than 30 mm. Hg. in the brachial artery of man. They believe "that Russell's contention that hypertonic contraction, and not high blood pressure is the cause of the high readings obtained with clinical instruments, has no basis in fact." At the same time they acknowledge that Russell has called attention to the influence of arterial contraction on clinical readings.

Russell<sup>13</sup> repudiates the statement in Janeway and Park's paper as misrepresenting his contentions.

#### *Nature of the present investigation.*

In the first part of this inquiry we have sought to determine, by hundreds of experiments on excised arteries, the behaviour towards compression of surviving arteries in contraction, relaxation, &c., both in the case of normal vessels and the altered vessels of old age and disease. We

have obtained a very large mass of data affording conclusive evidence in regard to certain features in the properties of such vessels taken from animals, the available supply of human arteries in suitable condition being very inadequate. Ordinary dead-house arteries provide no criterion of what the resistance of the wall of a living artery may amount to. The presence of considerable resistance in a dead artery, if such can be shown, would be very significant, for there is no evidence to suggest that the resistance could be less in the living state. But the absence of any appreciable resistance in the dead vessel would prove nothing as to what the living artery with its muscular tone, &c., might offer.

Much of the conflict of evidence on this subject appears to have arisen from the use of vessels in very different conditions, dead, living, relaxed, contracted, &c. In the earlier investigations dead arteries were used, both human and animal; comparatively few pathological arteries, even in the dead state, have been tested.

We have felt it to be of essential importance to use living arteries, not only in the healthy state but also in conditions of thickening and sclerosis. The possibilities in the shape of resistance to compression that may be offered by contracted and thickened arteries constitute the crucial question and the one of most urgent importance in regard to the reliability of blood-pressure readings under clinical conditions. In this connection we have largely availed ourselves of the use of arteries (especially the leg arteries) from old and diseased horses in which marked thickening of the muscular coat was commonly present.

We have found the investigation to be by no means so simple as might be imagined, and the sources of fallacy in some methods which we tested in the earlier stages of the inquiry were found to be of a serious character. Some of our earlier observations have been set aside on this account.

### *Methods.*

The resistance offered by the arterial wall to compression was examined in two conditions of internal pressure, (1) with a continuous or non-pulsatile stream, and (2) with a pulsatile stream through the vessel.

*Continuous stream.* The length of artery to be tested (after ligation of branches) had a glass tube tied into each end; after being tested for leakage (by air-pressure) it was placed in a glass compression tube similar to that used by Martin. At least 10-12 cm. of artery was subjected to compression, often 15-16 cm.; it is obviously important that a length at least equal to that compressed by the armlet used clinically should be employed. The arteries were tested as soon after death as was practicable; in the interval they were kept in defibrinated blood (oxygenated) in a vessel cooled by ice.



The internal pressure system was arranged in the following way. A stream of Ringer's fluid was passed through the artery at a definite pressure, read by a mercury manometer connected with the supply tube as shown in Fig. 1; it finally escaped through a glass tube drawn to a point so as to offer considerable resistance to the outflow. The supply tube comes from a bottle containing Ringer's fluid from which it is driven by air-pressure communicated from a large bottle into which water is allowed to flow from a reservoir elevated to a suitable level. (A ball-filler connected with the supply tube is useful for some experimental purposes, *e.g.*, getting up the pressure in the supply tube prior to beginning the flow from the upper reservoir, &c.). Another bottle supplies Ringer's fluid to surround the artery in the compression tube and apply pressure to it to test obliteration, &c.; this bottle was also connected with an Oliver's compressor for raising the pressure in the fluid surrounding the artery, the height of this pressure being shown by a second mercury manometer. This constitutes the external pressure system. The difference in height of the columns of mercury in the two manometers shows the excess of pressure outside the artery over that inside the vessel which is necessary for "obliteration," *i.e.*, to cut down the flow to a point corresponding with the abolition of the pulse wave when a pulsatile stream was used. In the arrangement we used, this point was indicated by a discharge from the nozzle at the rate of one drop per second.

When it was desired to test another fluid instead of Ringer's, *e.g.* solution of barium chloride adrenalin, &c., connections were made as indicated by the dotted lines at the upper part of Fig. 1.

*Pulsatile stream.* When a pulsatile flow was to be used, certain modifications were introduced into the foregoing arrangement. Rhythmical closure of the tube leading to the artery was provided for by an electromagnetic interruptor placed at the point marked X, the coils of this interruptor being in circuit with a clock which interrupted the electric current at a constant rate (*e.g.*, 60 per min.). In this way 60 pulsations per minute were produced in the stream passing through the artery. In some experiments a piece of highly distensible tubing was put in to represent an aorta, immediately after the interruptor. The interruptor is shown in Fig. 2.

Instead of the single Hg. manometer used with the continuous stream, a convenient arrangement of valved manometers (maximal and minimal) to show systolic and diastolic pressures and a "compensated" manometer (for mean pressure) was employed, being connected with the stream between the interruptor and the compression tube containing the artery and as near to the latter as possible. On the distal side of the compression tube a piece of relaxed artery (*e.g.*, carotid of sheep) was interposed, so that the pulse could be felt there and its disappearance and reappearance determined by the ordinary tactile method.\* The artery in the compression tube was tied on

---

\* When a continuous stream is used, this piece of artery must not be interposed; it would introduce a source of error by acting as an elastic reservoir.

glass tubes of similar and uniform calibre ; cannulas (with constricted necks) were avoided.

Sometimes in experiments with the pulsatile stream, air was substituted for Ringer's fluid as the compressing medium around the artery, to diminish the danger of interference waves being set up in the liquid around the artery (in certain circumstances, with very distensible artery, &c.) from the pulsation of the vessel. Interference of this sort was checked (when fluid was used) by temporarily turning off the stopcocks leading to the manometer and the pressure bottle.

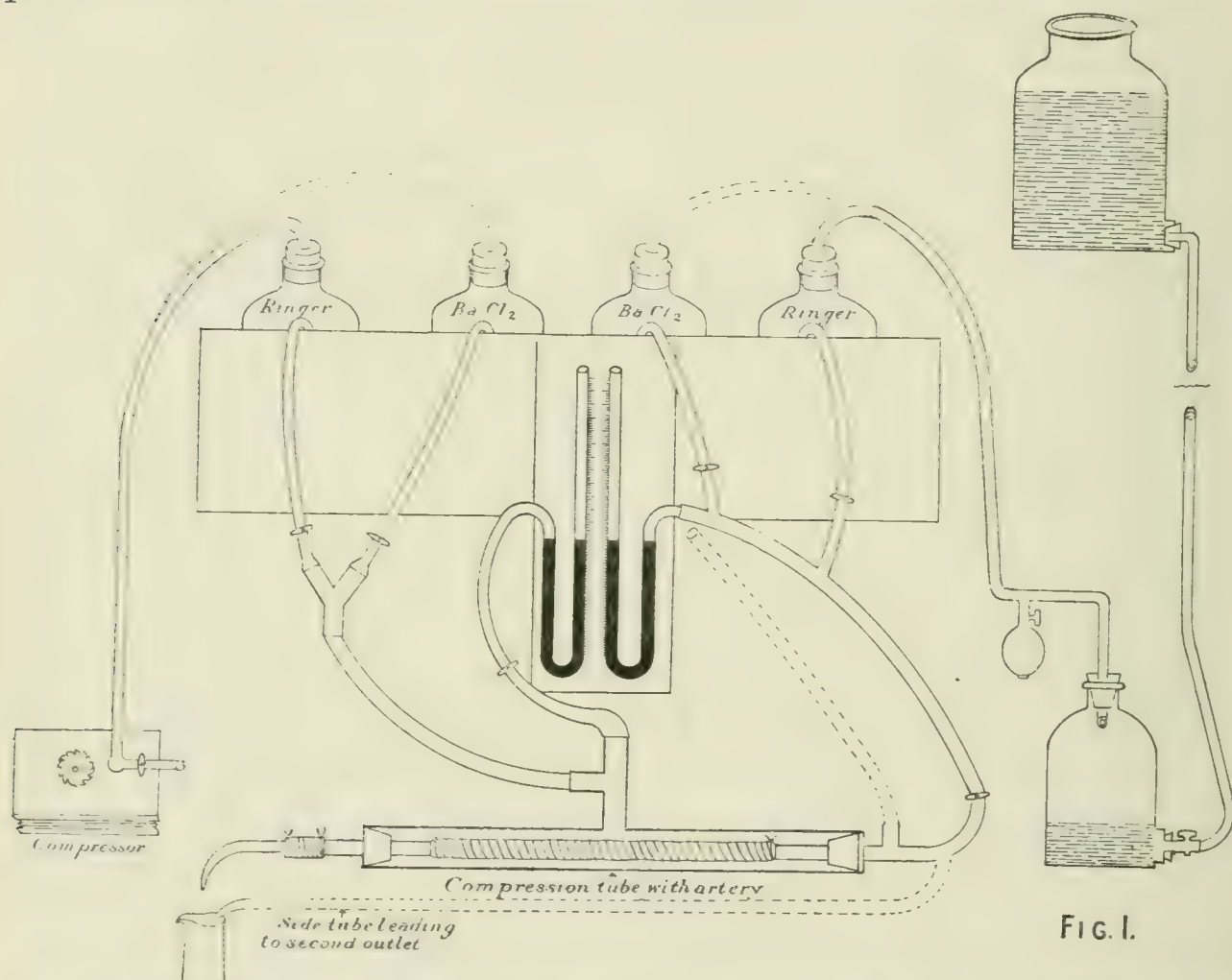


FIG. 1.

Fig. 1. Arrangement for testing obliteration pressure in arteries with (a) a non-pulsatile or (b) pulsatile flow of perfused fluid. The dotted lines indicate additional tubes necessary when a pulsatile system is to be used. The Hg manometer connected with the internal pressure system is then replaced by the arrangement of valved manometers mentioned in the text, not shown in the figure. The electro-magnetic interrupter is applied near the place marked X.

Much care was necessary in examining for leakage, in avoiding air locks from bubbles in the perfusing fluid, torsion of the arterial tube, &c. The vessel was placed in a state of moderate extension to imitate its state in a limb ; various degrees of extension were tried.

In some experiments instead of applying the obliterating external pressure to the artery through liquid or air in a compression tube as described above, we have supported the artery against a wooden "humerus" and



applied air pressure in the usual way through an armlet, the latter being either directly in contact with the artery or separated by animal tissues and an enclosing membrane, a sort of artificial "arm" round which the armlet was applied in the usual way.

Another plan was to embed the perfused artery in an animal's limb round which the armlet was applied in the usual way, and the obliteration tested as before. Care must be taken that the weight of a superincumbent mass of muscle does not press on the artery.

The results obtained by these methods were entirely confirmatory of those obtained with the compression tube, which was ordinarily employed.

*Comparison of continuous and pulsatile streams.* It was necessary to compare these very carefully so as to obtain a definite index of pulse obliteration which could be applied to the continuous stream. Complete stoppage of flow would obviously not afford any valid criterion, as the transmission of the pulse must be blocked in the compressed area before the flow is completely arrested.

An artery showing an ascertained and constant resistance was tested for the obliteration point by the tactile method, while a pulsatile flow was going on; the amount of external pressure necessary to stop the pulse being thus determined, a continuous stream was substituted for the pulsatile one and the same external pressure as before applied; it was found that the flow was not arrested, perfusion fluid still escaping from the fine-pointed outlet tube or nozzle at the rate of one drop per second, determined by comparison with a metronome. Of course the rate of dropping would vary with the size of nozzle employed; with the one we used the rate stated served as a very definite pulse-index—the pulse-disappearance index (visual method).\*

The pulse-reappearance index is a definite acceleration of the rate of dropping from the one per second standard. This always came at a lower level of external pressure, the amount of the lowering varying according to circumstances, the condition of the artery, the height above the obliteration point to which the external pressure was raised, and the time it was kept up before the lowering began. With our experimental arrangement, when we raised the external pressure only just enough to give the pulse-disappearance index and at once began lowering carefully the pulse-reappearance index usually showed at a few mm. below the other, *i.e.*, the difference between the two indices was trivial, at least in arteries not showing much resistance.

On the other hand when the external pressure was run up far above the pulse-disappearance level and kept up for some little time before being lowered, with contracted arteries, the pulse-reappearance index came at a much lower level. The conditions in such a case approach those present when repeated compression or prolonged compression is employed, with effects described later. Thus an artery which showed a difference of 30 mm.

---

\* Oliver's screw-compressor is very convenient for accurately graduating the external pressure. The continuous stream used is at the same pressure as the systolic pressure in the pulsatile stream.

between disappearance and reappearance when the external pressure had been kept up for one minute before reappearance was allowed, showed only slight differences (*e.g.*, 2-5 mm., &c.) when the lowering of the external pressure was begun immediately after the point of disappearance.

The method of the continuous stream we employed very largely; amongst other things it obviates the possibility of alterations in the resistance of the arterial wall being complicated by altered conduction of the pulse wave in a more contracted or less contracted artery, when the pulsatile stream was used. This is of importance in testing the effects of repeated compression of an artery on its obliteration pressure; with a continuous stream altered readings must be ascribed to changes in the resistance which the arterial wall offers to compression.

A comparative experiment on the carotid of the ox is here given:

| NATURE OF FLOW. |    | INTERNAL PRESSURE.<br>(MAXIMUM) | OBLITERATION PRESSURE. |          |
|-----------------|----|---------------------------------|------------------------|----------|
|                 |    |                                 | (TACTILE)              | (VISUAL) |
| Continuous      | .. | 130                             | —                      | 140      |
| Pulsatile       | .. | 126                             | 140                    | 140      |
| Pulsatile       | .. | 122                             | 132                    | 130      |
| Continuous      | .. | 120                             | —                      | 128      |

The resistance of the arterial wall here comes out as 8-10 mm., by the visual method with a continuous flow, and as 8-14 mm. by the tactile method with a pulsatile flow.

In a sheep's carotid showing very slight resistance with a systolic internal pressure of 146, the tactile gave 150 for the disappearance and 148 for the reappearance of the pulse, the same pressures gave drops from the nozzle at the rate of one drop in about a second with disappearance and at a definitely quickened rate with reappearance of the pulse.

The test by a pulsatile stream differs from that performed with a non-pulsatile stream in regard to the influence of constriction of the arterial lumen upon the obliteration readings. Excessive constriction beyond a certain point diminishes the systolic wave along the arterial tube leading to the place of obliteration, and so makes the pulse disappear at a lower level of external pressure; in this way extreme constriction acts in the opposite direction to that of the increased resistance of the contracted arterial wall with the result that the influence of the latter upon the obliteration reading may be diminished by the former. Under such conditions the indications yielded by the continuous stream are not identical with those given by the pulsatile arrangement, the former giving higher readings than the latter.

We have experimented with tubing of different sizes and have obtained results from which we conclude that with blood-pressure estimations made on such an artery as the brachial this factor is not of practical importance. We compared the influence of equal lengths of tubing of very different calibres placed in the course of the stream going to the artery in the compression



tube, and found no appreciable effect except with diminutions of calibre that are not applicable to the vascular channel leading to the seat of brachial compression.

When the pulsatile and the continuous stream gave similar results in an artery in the contracted and relaxed states, it is evident that no appreciable part can be played by altered conduction of the systolic wave in the contracted as compared with the relaxed tube.

Again, when a contracted artery is softened at one spot (*e.g.*, by crushing with a forceps for a length of 3-5 mm. or so) the resistance to compression will be reduced to the small amount offered at the weak spot, while there can be no appreciable change in the conduction from the softening of so very limited an area, the (comparative) rigidity of the rest of the tube remaining unchanged.

It is perhaps hardly necessary to remark that the use of water as a perfusing fluid is inadmissible. In the case of living arteries very extensive changes are caused by water, stiffening and extreme contraction, change in colour, &c. The contraction may be so excessive that the lumen of even a large artery may be nearly closed; we found that a carotid from the ox showing a lumen of 5-6 mm. when relaxed, became so constricted that the water (under a pulsating pressure comparable to blood-pressure) only came through in drops.

In the case of dead arteries, with which water has been used by some investigators, its physical effects are not marked, though its employment is obviously undesirable.

We may refer to the importance of using valved manometers when working with a pulsating stream. The Hg. manometer which has sometimes been used, shows neither systolic nor diastolic pressure correctly, the nature and extent of the errors varying with the rate of pulsation, &c. No accurate readings, except of mean pressure can be got from a pulsating stream by its use, unless suitable valves are interposed.

#### *Types of artery examined.*

The arteries examined were taken from various animals\* (horse, ox, sheep, cat, &c.), as soon as possible after death. When excised they were left embedded in the surrounding tissues and put into oxygenated defibrinated blood or Ringer's solution till about to be examined. If not tested at once, they were kept in these fluids in a cold safe. Vitality was exceedingly well maintained for long periods, active responses to stimulation being manifested, after days, &c., in many cases, especially in the horse's arteries.

---

\* The human arteries (of sufficient length) which we have examined were not possessed of sufficient vitality for testing their resistance in a strongly contracted state. In the relaxed state their resistance was trivial (1-2 mm., &c.).

In the necessary ligaturing of branches, very numerous in some arteries, care was taken to avoid injury or distortion of the vessel wall by tying the branches a little distance from the main tube. It is obvious that local injury even if very limited would vitiate the obliteration test, as the weakened part would naturally become closed so as to obstruct the stream before the rest of the tube has been compressed.

*Carotid of ox, horse and sheep.* We have performed many experiments on carotids of the ox and sheep, and a smaller number on that of the horse.

The carotid of the ox is so different in size and thickness of wall from the normal human brachial that numerical values obtained from the former cannot reasonably be transferred to the latter. But large strongly-muscular arteries like these carotids can be usefully employed in the study of various properties of the arterial wall, its relative resistances in the living and dead and in the contracted and relaxed states, the effects of warming and cooling, drugs, repeated compression, comparison of continuous and pulsatile stream, relation of size of lumen to resistance of wall, &c. The normal carotid of the sheep more nearly resembles the normal human brachial and can be more fairly taken to give comparable numerical values as regards obliteration readings in various conditions.

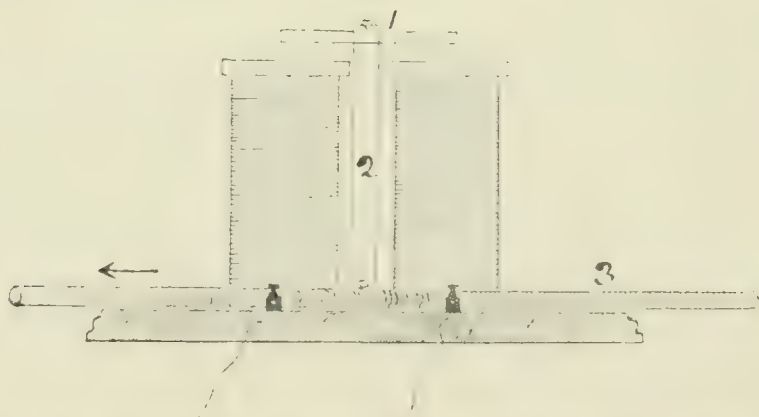


Fig. 2. Electro-magnetic interrupter for giving a pulsatile stream. Each time the current is made by a clock the horizontal steel bar (1) at the top is drawn downward by the electro-magnets and a vertical rod (2) connected with it presses on a soft rubber tube (3) conveying the perfusion fluid and temporarily occludes it, usually 60 times per minute.

The *metacarpal* and *metatarsal* arteries of the horse are very important for experimental purposes in this connection, as they can be obtained from old and diseased horses in various conditions of thickening, &c., while they retain their vitality long, responding actively to stimulation after days, when kept in suitable conditions.

The following measurements taken from such arteries will indicate their relative dimensions. We must emphasise the importance (still insufficiently realised) of ensuring complete relaxation in arteries to be measured; otherwise no accurate comparison can be made and widely varying measurements may be got from the same vessel, varying amounts of contraction entirely altering the size of the lumen, thickness of wall and



middle coat, &c., as described by one of us (J. A. MacWilliam) in conjunction with A. H. Mackie, a good many years ago. We have ensured relaxation in some of the various ways described by one of us: most commonly by keeping in 1% sodium fluoride solution or boiled Ringer's solution with a little arsenious acid for some days at room temperature or for a day at 38° C., by ammonia vapour, sulphocyanide, &c., or by manipulation (kneading).

We believe that from neglect of this precaution very misleading conclusions are sometimes arrived at as to thickening of the arterial wall, middle coat, &c.

---

|                           |    |    |    |    |       |     |
|---------------------------|----|----|----|----|-------|-----|
| <i>Brachial, human.*</i>  |    |    |    |    |       |     |
| Inner coat ..             | .. | .. | .. | .. | 0.03  | mm. |
| Middle ..                 | .. | .. | .. | .. | 0.50  | ..  |
| Outer ..                  | .. | .. | .. | .. | 0.25  | ..  |
| Total thickness of wall   |    |    |    |    | 0.78  | ..  |
| Lumen ..                  | .. | .. | .. | .. | 4.17  | ..  |
| <i>Carotid, sheep.</i>    |    |    |    |    |       |     |
| Inner coat ..             | .. | .. | .. | .. | 0.028 | ..  |
| Middle ..                 | .. | .. | .. | .. | 0.429 | ..  |
| Outer ..                  | .. | .. | .. | .. | 0.168 | ..  |
| Total thickness of wall   |    |    |    |    | 0.616 | ..  |
| Lumen ..                  | .. | .. | .. | .. | 3.0   | ..  |
| <i>Metacarpal, horse.</i> |    |    |    |    |       |     |
| Inner coat ..             | .. | .. | .. | .. | 0.03  | ..  |
| Middle ..                 | .. | .. | .. | .. | 0.513 | ..  |
| Outer ..                  | .. | .. | .. | .. | 0.31  | ..  |
| Total thickness of wall   |    |    |    |    | 0.853 | ..  |
| Lumen ..                  | .. | .. | .. | .. | 2.7   | ..  |
| <i>Carotid, ox.</i>       |    |    |    |    |       |     |
| Inner coat ..             | .. | .. | .. | .. | 0.084 | ..  |
| Middle ..                 | .. | .. | .. | .. | 1.176 | ..  |
| Outer ..                  | .. | .. | .. | .. | 0.481 | ..  |
| Total thickness of wall   |    |    |    |    | 1.744 | ..  |
| Lumen ..                  | .. | .. | .. | .. | 6.0   | ..  |

---

### *Relaxation and contraction of arteries.*

Keeping for some time at 38°-40° C. in defibrinated blood or Ringer's fluid is the simplest mode of obtaining relaxation, and perhaps the most unobjectionable one, in arteries arranged for experiment. This method is generally successful, but not always; in some instances a considerable amount of contraction persists after the vessel has been kept at body

---

\* The wall measurements of the brachial here stated are nearly identical with those given by Ballance and Edmunds ("Ligation in Continuity," p. 46, 1891). These writers do not state the size of the lumen and we have not seen any very definite records of this, though no doubt such exist. In Quain's Anatomy (10th ed. ii, 378) it is stated that the "average calibre" of the brachial is 6 mm. Vierordt (Anat.-Physiol. u. Physikalische Daten u. Tabellen, 1906) puts the diameter at 7 mm. at its beginning and 5.6 mm. at its end. It is not stated whether external or internal diameter is meant. These measurements are apparently of external diameter; the use of the term "calibre" in this sense is misleading.

temperature for 15-30 min. or longer. Manipulation of an artery (rolling between the fingers, &c.), repeated compression, &c., also have relaxing effects.

There are other means of obtaining complete relaxation, but they usually involve the death of the arterial muscle, *e.g.*, keeping in blood or Ringer's fluid or 1% sodium fluoride in a warm chamber at body temperature overnight, or in 1% sodium fluoride at room temperature for longer periods (days). Ammonia vapour and strong sulphocyanide solutions are powerful and rapid relaxing agents but they induce other changes in the arterial wall.

Contraction is generally very strongly present when the artery is prepared and placed in the compression tube to be tested, at room temperature. In opposition to the generally accepted belief, we do not find that cold *per se* causes arterial contraction, whether it be cooling to room temperature or down to the freezing point. Nor does exposure to the air have much, if any, effect. The importance of a cold or cool temperature (*e.g.*, room temperature) is that when a surviving artery is brought under the influence of the mechanical irritation of cutting, handling, &c., cold favours the contraction and renders it persistent for long periods (days), commonly indeed until the vitality of the arterial muscle fades. The significance of a relatively low temperature in this connection is shown by the effect of restoring the artery to body temperature, the persistent contraction generally becomes relaxed, to contract again on cooling.

We have seen no reason to believe that the stiffness and resistance of a strongly contracted cold artery are due to any influence of the cold other than its power of determining the persistence of contraction of various degrees of intensity. We are not aware of any evidence to show that a certain degree of contraction in the cold state makes an artery stiffer or more resistant to compression than the same amount of contraction induced by other influences in a warm artery. A dead or an uncontracted surviving artery shows no differences of that sort in the cold as compared with the warm state. Arteries which fail to show much contraction at room temperature, as is sometimes seen in the carotid of the horse and more rarely in that of the ox, then give quite low readings, even such large vessels as the ones mentioned.

To induce contraction in the artery kept at body temperature, adrenalin and barium chloride were the agents most commonly used, the latter in strengths varying from 0.5% to 2.5%. In some cases an isotonic mixture of the chlorides of barium, sodium, calcium and potassium, the barium predominating, was tried. It was only in exceptional cases that arteries kept at body temperature showed marked contraction without the use of any of the preceding agents.

In many experiments the obliteration value of the arterial wall (*i.e.*, the excess of external over internal pressure required to cause obliteration) was first tried at room temperature, then at body temperature, and lastly under the influence of the vaso-constricting solution, the fluids of the internal



and external pressure systems (*i.e.*, inside and outside the artery) being at the same temperatures (cold or warm) in each case.

*Measurements of the resistance to compression offered by the arterial wall in different conditions.*

The obliteration values obtained from relaxed arteries were in all cases small, whether such large vessels as the carotids of the ox and horse were used or smaller ones (*e.g.*, carotid of sheep, metacarpal of horse) more closely comparable with the arteries used for clinical estimations. An excess of a few millimetres of external pressure over the internal pressure usually sufficed to close the vessel so as to obliterate the pulse. In many cases, in the smaller arteries especially, a resistance of the vascular wall in this condition only amounted to 1-2 mm. Hg..

These low values agree with those obtained by some former observers, such as von Basch and Martin, who had evidently worked with relaxed and presumably dead arteries.

In contracted arteries very extensive differences were found, varying with the amount of muscular contraction present. It is clear that the very high figures sometimes obtained were really dependent on muscular contraction and not on resistance to compression offered by the other elements of the vascular wall. For as soon as muscular contraction was removed by any of the diverse methods employed for that purpose, the resistance invariably fell to very low figures, quite unimportant as regards their clinical significance. The various methods used to induce muscular relaxation often had effects on the arterial wall differing much in detail, but agreeing in the fact of removing muscular contraction and, concurrently, the great bulk of resistance to compression.

The highest values for arterial resistance were naturally found in vessels in a state of persistent and powerful contraction at room temperature.

*Carotid, ox.* In the contracted state at room temperature common values were 20-60 mm. Hg., but occasionally they run very much higher. In some instances such enormous resistances were found that pressures of 150, 160 and 186 mm. were required to overcome the resistance of the arterial wall and stop the flow through it in the degree corresponding to abolition of the pulse. Similar results were obtained with the non-pulsatile and the pulsatile stream. The great resistance was due almost entirely to the muscular contraction and not to a permanent stiffness of the arterial tube. This is illustrated by the fact that the artery showing a resistance of 150 mm. at room temperature had only a resistance of 18 mm. at body temperature, while the one with an initial resistance of 186 mm. at room temperature gave such low values as 16, 6 and 1 mm. when repeatedly tested at 38° C..

Tested at body temperature, the highest reading obtained from a contracted ox carotid was 64 mm., in an artery which remained persistently contracted while warm without the application of any drug.

With contraction excited by barium chloride, the highest resistance noted was 63 mm..

*Carotid, sheep.* The resistances observed with this artery may be summarised as follows :—

Relaxed at body temperature, a nominal resistance, *e.g.*, 1 mm..

Contracted at room temperature, all sorts of figures up to 30 mm.; common values, 10-20 mm..

Contracted at body temperature (barium chloride, &c.), various readings up to 35 mm.

*Metacarpal and metatarsal of horse* sometimes showed an enormous resistance, values over 100 mm. in some cases, *e.g.*, 108, 114, 116, 130 mm..

In some of these cases the arterial wall, especially the media, was greatly thickened and the lumen was relatively small, but this was not invariably the case. An extraordinarily high resistance was sometimes got in a very strongly contracted artery which when relaxed gave practically normal measurements of lumen and wall, *e.g.* lumen about 3 mm., wall about 1 mm. There was no evidence of calcareous change in any of these vessels.

In the fully relaxed state under the influence of warmth, &c., the horse's arteries examined gave slight resistances, often only a few mm. Hg., there being an extraordinary range between the powerfully contracted vessel at room temperature and the same when relaxed. Thus the resistance of 116 mm. shown to begin with by a metacarpal at room temperature, came down to 3-5 mm. when relaxed at 38° C., though sometimes the remaining resistance was higher than this, *e.g.* 18-26 mm..

At body temperature under the influence of barium chloride various figures were obtained up to 60 mm.—nothing at all approaching the resistances sometimes seen in the cold. The observations were complicated in a good many instances by the tendency of these vessels to close up altogether under the influence of stimulation, so that little or no external pressure was needed at certain phases to stop the flow. This was sometimes seen in an artery, which a short time before (with a lumen of 0.5 mm. or so) showed an extremely high resistance to compression.

It is to be specially noted that the maximal readings stated above were all much above the general level. They were obtained by using the pulse-disappearance index at first compressions; with the pulse-reappearance index lower, and with second compressions much lower, figures were got. Some illustrations of such differences are given later in dealing with the effects of repeated compression.

We cite the results obtained at room temperature to show the very remarkable resistance to compression which arteries *may* exhibit in certain conditions. It is of course obvious that these conditions of temperature are widely removed from those present under clinical conditions, and we naturally do not wish to be understood as assuming the existence of such degrees of contraction and their concomitant resistances in the human body.



There is another factor that comes into play in affecting obliteration readings—the influence of extreme constriction, as has already been stated in comparing the methods in which a pulsatile and a non-pulsatile flow respectively are used. But this does not seem to be such as to have any practical bearing on brachial estimations.

*Influence of soft portions in the course of an otherwise resistant artery.*

Russell<sup>13</sup> has argued against the idea of soft parts in the course of an artery under compression negating the resistance of the more rigid tube and has advanced the view that the compressing bag of the armlet must bridge over these soft portions.

We have tested this point experimentally by embedding a contracted carotid (ox) in a portion of an animal's limb\* (*e.g.*, hind limb of ox) in such a way that when an armlet was applied in the usual way, the carotid was compressed against the bone, as the brachial is compressed against the humerus. Fluid was perfused through the artery as before, the arrangement just described taking the place of the glass compression tube shown in Fig. 1. A very limited local softening of the contracted and resistant arterial wall was produced by firmly pinching the artery across at one place between the blades of an artery forceps in order to break down the resistance of the arterial wall. The strictly localised nature of the softening so produced (3-5 mm.) was evident when the vessel was subjected to internal pressure, the softened part yielding more and showing as an annular dilatation.

The obliteration pressure was then tested in the usual way by (1) the continuous, and (2) the pulsatile stream, and the influence of the arterial wall was found to be negligible (a few mm.). Next the softened area was protected from compression by a short piece of rigid tubing (of sufficient length to cover the local softening) being slipped over it. The obliteration pressure was then found to have gone up strikingly, the excess of external over internal pressure (*i.e.*, the resistance of the arterial wall) amounting to over 40 mm.

The protecting tube was then removed and the arterial resistance found to be negligible. Repeated observations of this kind gave a repetition of similar results, the actual value of the arterial resistance, as shown when the softened part is protected, becoming successively lowered, as usual, by the repetition of the compression. These very definite and convincing results make it plain that the inflated bag of the armlet acts effectively on a very limited soft portion of an artery and prevents the resistance offered by the rest of the tube from affecting the obliteration readings much.

Instead of using an armlet in the way described, we have also tried contracted arteries in the compression tube in the usual way before and after a very limited (3 mm.) area of softening had been artificially produced. The high resistance at first shown was suddenly cut down to a vastly greater

---

\* Care must be taken that no weight of superincumbent muscle presses on the artery.

extent than usually occurs with a second compression, *e.g.*, from 48 to 13 mm., tested by reappearance of pulse. With a very narrow ring of softening one would hardly expect the influence of the arterial wall to be quite nullified, at least in a very large artery, even though the resistance at the narrow ring were completely removed, in view of von Recklinghausen's\* observations on the influence of the length of tube to which the obliterating force is applied. Obliteration of a narrow ring of tube involves something of a pull upon the adjacent resistant parts.

*Relation of the resistances experimentally found to the degrees of contraction which may be found in the circulation.*

This is a difficult question upon which much light is needed from the clinical side. Experimentally we have tried to get some sort of clue on the following lines.

It is clear that when the pressure within an artery does not distend it to or beyond the size of the passive tube (while empty or at zero pressure) the muscular tone of the vessel must be sufficient to counterbalance the distending force of the internal pressure; if it were insufficient the arterial wall would yield further, if it were stronger, the vessel would contract more.

We have got arteries in such a state of contraction as to balance in this way internal pressures comparable to blood-pressures, as tested in a pulsatile scheme. The artery is then tested for the resistance of wall to obliterating pressure.

A sheep's carotid was found to be in a state of contraction that kept it of a diameter just below its diameter (5 mm. externally) in the passive relaxed condition, when exposed for some time to an internal systolic pressure of 100 mm., diastolic 58 mm.; tested for obliteration in the usual way the resistance of its wall was found to be about 15 mm.. Another carotid (sheep) which had been tested with somewhat higher internal pressures gave a wall resistance of 17 mm.. In other words such resistances as these were found to be associated with a degree of muscular tone just sufficient to balance pressures something like blood-pressure, not allowing expansion beyond the size of the passive tube and not strong enough to cause constriction below that size.

An ox carotid which was sufficiently contracted to resist an internal pressure of 140 mm. systolic and 130 mm. diastolic without being distended quite to the size of the passive tube gave by the obliteration test a resistance of 57 mm.

We cite the numerical values obtained in these comparative experiments with a certain amount of reserve on account of the fact that they were done at room temperature, it being less difficult to get a relatively constant degree of contraction persisting for a considerable time at this temperature than at body temperature. We are not convinced that any error was introduced in this way; there is no evidence to show that the relation between resistance to distension by internal pressure and to compression by external pressure is influenced by room temperature as compared with body temperature.

---

\* Arch. f. exp. Pathol. u. Pharmacol. 1901, xlv, 78.



In any case it may be safely deduced from these experiments that if the readings are at all moderate, no grave error can have been introduced into them as indications of blood-pressure by the action of the arterial wall, provided the artery is not definitely constricted, *i.e.*, below the size of the passive tube.

*Effects of repeated compression.*

In the case of completely relaxed or dead arteries showing very little resistance to compression, repetition of obliteration naturally makes no appreciable difference.

But in arteries showing a high resistance from muscular contraction repeated compression has very notable effects in reducing the value of the arterial wall, with varying rapidity in different cases. The reduction may go on more or less steadily till the arterial resistance has been cut down to practically the value of the relaxed wall, or it may stop short or tail off far above this point, after effecting a marked lowering. Much depends on the state of the arterial muscle, as well as on the number of compressions and the height to which the compressing pressure is raised, the duration of each, and the intervals between them. With long intervals the vascular wall may recover to a considerable extent between them, and the total effect of a certain number of compressions may be much less than if the compressions came in quicker succession. Thus an artery resistance which had come down on repeated compression from 35 mm. to 9, rose again to 31 mm. after a 15 min. interval.

So constant and striking is the effect of repeated compression that it serves as an effective test for the presence or absence of appreciable resistance offered by the arterial wall. It is very noteworthy that a higher reading never seems to be obtained ; when there is any change it is always a lowering.

---

*Metacarpal of horse. 3½ hours p.m.*

Contracted at room temperature. Tested by continuous stream.

| OBSERVATION. | INTERNAL PRESSURE. | EXTERNAL PRESSURE. | ARTERIAL WALL. |  |
|--------------|--------------------|--------------------|----------------|--|
| 1            | 104                | 218                | 114            |  |
| 2            | ..                 | 160                | 56             | When contracted, lumen was 0.5 mm. and wall over 2 mm.. Later after relaxation lumen was 3 mm. and wall 1 mm.. |
| 3            | ..                 | 140                | 36             |  |
| 4            | ..                 | 140                | 36             |  |
| 5            | ..                 | 130                | 26             |  |

*Another piece of artery.*

|   |     |     |    |
|---|-----|-----|----|
| 1 | 104 | 200 | 96 |
| 2 | ..  | 164 | 60 |
| 3 | ..  | 162 | 58 |
| 4 | ..  | 160 | 56 |

*Metacarpal from another horse.*

Contracted at room temperature. Tested by pulsatile stream. Disappearance and reappearance of pulse determined by tactile method. The values of the arterial wall by the two methods are given.

| OBSERVATION. | INTERNAL PRESS. SYSTOLIC. | PULSE DISAPP. | ARTERIAL WALL. | PULSE REAPP. | ARTERIAL WALL. |
|--------------|---------------------------|---------------|----------------|--------------|----------------|
| 1            | 104                       | 164           | 60             | 150          | 46             |
| 2            | ..                        | 158           | 54             | 148          | 44             |
| 3            | ..                        | 154           | 50             | 138          | 34             |
| 4            | ..                        | 146           | 42             | 136          | 32             |

---

Instead of repeated compressions with a lowering of the pressure between each one may use a continuance of the obliterating pressure for some time (*e.g.* 2-3 min. or more). This has effects similar to a series of compressions. Thus in an ox carotid showing a wall resistance of 160 mm. both by pulsatile schema and continuous stream (internal pressure 40, obliterating pressure 200 mm.) after compression of a limited area of the vessel between finger and thumb for 3 min. the next test showed that the resistance of the arterial wall had fallen to 100 mm.. The vessel in the compression tube was plainly seen to become flattened at the spot which had been previously compressed, while there was no flattening elsewhere. This fall of 60 mm. was much more than would be expected to follow a second rise of the external pressure apart from the influence of the continued local compression. The next test showed a fall of 20 mm. and several further tests showed no further fall. We have applied the same method clinically, sometimes intermitting the pressure rapidly to avoid ischæmia of the limb.

*Question of resistance not due to contraction.*

A lowered resistance also follows the use of repeated or continued compression in the case of dead arteries which owe their resistance to causes other than contraction of their muscular coat, *e.g.*, stiffening due to the action of certain chemical agents (formalin, &c.); change of the tube from the circular to the oval or flattened form renders subsequent compression easier, provided time has not been allowed for recovery of the circular form, even apart from changes in the physical condition of the tissues caused by the preceding distortion.

But we have not, so far, in the course of our work met with arteries showing any marked resistance to compression (when tested in the ways described) apart from the presence of muscular contraction.\* In the cases just referred to we had purposely induced changes in the physical characters of the vascular wall that have had no parallel in any of the arteries (animal or human) that have come to our hands. Still the fact that repeated or continued compression can reduce a resistance not due to muscular contraction is important, for it shows that this method affords no means of discrimination between resistance due to muscular contraction and at least some forms of resistance due to other causes, if such are ever present in human arteries under the conditions of blood-pressure estimation.

The similarity of behaviour between a living contracted artery and a dead one rendered resistant by formalin extends to the partial recovery of resistance after an interval.

The results in such an artery are shown in the following experiment. Carotid (ox) relaxed and dead, treated with 10% formalin for half an hour.

---

\* The great bulk of available evidence is opposed to the idea of thickened arteries offering any important resistance, apart from the presence of muscular contraction; this is in agreement with the results of von Basch, Martin, Janeway and Park and others working with dead sclerosed arteries. The only positive piece of evidence in the contrary sense is that advanced by Herringham as already mentioned; his results were obtained from dead arteries.



Tested with continuous stream, increase of flow to the pulse-reappearance index (after obliteration) being taken as the gauge.

---

| Internal pressure 120 mm. |     |            | Internal pressure 110 mm. |     |            |
|---------------------------|-----|------------|---------------------------|-----|------------|
|                           |     | ART. WALL. |                           |     | ART. WALL. |
| (1)                       | 200 | .. 80      | (9)                       | 142 | .. 32      |
| (2)                       | 190 | .. 70      | (10)                      | 136 | .. 26      |
| (3)                       | 170 | .. 50      | (11)                      | 128 | .. 18      |
| (4)                       | 156 | .. 36      | (12)                      | 128 | .. 18      |
| (5)                       | 132 | .. 12      | (13)                      | 122 | .. 12      |
| (6)                       | 128 | .. 8       | (14)                      | 118 | .. 8       |
| (7)                       | 124 | .. 4       | (15)                      | 118 | .. 8       |
| (8)                       | 124 | .. 4       | (16)                      | 116 | .. 6       |

---

Interval of 15 min.

The progressive decline in the resistance on repeated compression is very evident, also the partial recovery after a pause of 15 min., followed again by a decline on further recompression.

### *Spasmodic closure of arteries.*

The surviving metacarpal or metatarsal artery of the horse sometimes contracted so strongly and extensively that the lumen became entirely obliterated, and very high pressures were inadequate to force fluid through the vessels, pressures as high as 440 mm. Hg. being sometimes tried without effect.

Thus in an excised metacarpal (examined 23 hours p.m.) strong contraction was present and the lumen was very small (0.5-1.0 mm.); when mechanically stimulated by cutting, the tube closed entirely so that absolutely no flow could be got through it at a perfusion pressure of 300 mm.

When a bristle was pushed into the vessel, against considerable resistance, for a distance of 30 mm. it was so firmly grasped by the arterial muscle that a weight of 20 grammes was needed to pull it out: this was determined by connecting the bristle to one arm of a balance and gradually weighting the other arm, just sufficiently to draw out the bristle. Keeping the artery at 38°-40° C. for 15 minutes or more quite failed to induce the usual relaxation or to lead to the passage of any fluid at a pressure of 250 mm. Hg. in the supply tube.

Later, when relaxed, this artery was found to have a very thick wall and a small lumen; wall 1.75-2.0 mm., lumen 2 mm..

In the case of another horse a piece of metacarpal artery (3 hours p.m.) relaxed completely when perfused at body temperature, and then the resistance of the arterial wall was only 1-2 mm. Hg..

Another piece of the same artery became so extremely contracted when cut, &c., at room temperature that when a bristle was with difficulty pushed into the lumen for 30 mm. it was gripped so firmly that a weight of 30 grammes was required to draw it out.

A third piece arranged for perfusion and testing in the usual way closed its lumen so firmly that it was impossible to obtain any flow through the vessel even when the pressure of the perfusion fluid was raised to 440 mm. Hg..

External pressure (as usually employed to cause obliteration) was then applied up to 160 mm. Hg. and this pressure was kept on for some minutes. It was then found possible to get a flow through the artery when the perfusion fluid was raised to 380 mm. Hg.; later at 105 mm., the stream being again stopped by an external pressure of 50 mm..

Some time later the perfusion fluid flowed slowly through at so low an internal pressure as 10 mm., there being no external pressure applied at that time.

It is of course well known that in such conditions as Raynaud's disease arteries of small size contract to such an extent as to obstruct the blood-supply seriously. And various writers account for the occurrence of transitory aphasia, paralysis and other disturbances of nervous function by the hypothesis of a temporary ischæmia depending on spasmodic contraction of the middle cerebral artery or some of its branches. These however are small vessels compared to the horse's metacarpal and metatarsal. Such closure as we have described is no doubt associated with the phenomena attributable to intermittent claudication that have been observed in the horse and in man. We have seen an approach to a similar condition in a still larger artery, the carotid of the ox, but only in very abnormal circumstances, when perfused with water as already referred to. In a smaller artery from the hind limb of a presumably healthy ox we have noted closure on cutting, &c., at room temperature; 14 grammes were needed to pull out a bristle which had been passed in for 30 mm..

In the closure of the horse's arteries above described this evidently involved a very unusual and extreme degree of shortening of the muscular fibres of the tunica media. An enormously thickened intima might of course determine closure without such extreme contraction, but sections showed that such an explanation was not valid, there was little or no intimal thickening.

From the foregoing evidence it is clear that the horse's leg arteries sometimes show extraordinarily wide variations in their behaviour, the same artery (a) when relaxed offering a merely nominal resistance to compression, (b) when strongly contracted with thick wall and small lumen (0.5-1 mm.) requiring an exceedingly high external pressure to obliterate its channel, and (c) when powerfully contracted in such a way as to close the lumen resisting the passage of fluid through it even when supplied at enormous pressures. So far as our experience goes the arteries in which complete closure has occurred have all been abnormally thick-walled, with extensive thickening of the media. The wall thickness sometimes stood to the lumen as 1 : 1, 1 : 1.33, 1 : 1.6, &c., instead of the ratio of 1 : 2.5-3.0, &c., seen in arteries in more approximately normal conditions from horses' legs.



## CONCLUSIONS (PART I).

In investigating the part played by the arterial wall in relation to the estimation of systolic blood-pressure by the obliteration method it is essential to use surviving arteries in different conditions of contraction and relaxation, and to test abnormal and thickened arteries as well as normal ones; the question cannot be settled by a study of ordinary dead-house arteries or even of normal living arteries.

Relaxed arteries whether normal or thickened have in the instances examined given very inconsiderable resistances to compression, usually not more than a few mm. Hg..

Contracted arteries show resistances varying with the amount of contraction present. Arteries powerfully contracted at room temperature may give high values, rising sometimes to over 100 mm. Hg. in the metacarpal or metatarsal artery of the horse and in the carotid of the ox. Arteries contracted at body temperature yield much lower figures, a maximum reading of 35 mm. for the carotid of the sheep, 64 mm. for that of the ox and 60 mm. for the metacarpal of the horse. These are maximal values obtained at the first compression by the pulse disappearance index; with the pulse reappearance index at the second compression the values are much lower. Arteries offering great resistance when strongly contracted show very little when fully relaxed.

When contraction causes extreme constriction of the arterial lumen below a certain point the transmission of the systolic wave to the seat of compression may be diminished, and this factor may lessen the effect of the increased resistance of the arterial wall upon the obliteration readings, in arteries capable of having their lumen reduced to a minute size.

Thickened metacarpal and metatarsal arteries from old horses often contract so much as to close their lumen completely and resist any passage of fluid through them even at pressures up to 440 mm. Hg..

Repeated compression or continued local compression, while not appreciably affecting the readings from normal arteries under ordinary conditions, has an important effect in reducing the resistance of a contracted artery, and may be used as a means of ascertaining the presence or absence of abnormal resistance in the arterial wall. Massage of a resistant artery may be used with similar effects.

## PART II.

The results obtained from the study of excised living arteries examined under definite conditions are important in showing what influence may be exercised by the arterial wall in different conditions. There remains the correlation of these conditions with what may be present in the individual cases examined clinically.

The lines on which we have sought to attack the clinical problem are the following :—

(1) Comparison of the characters of clinical arteries with living excised arteries of comparable size, in different conditions as regards thickening, contraction, &c.

(2) A study of the effects of repeated or continued compression.

(3) Comparison of the indications obtained from the two arms, arm and forearm, &c.

*Comparison of clinical arteries with excised arteries.*

We need do no more than refer to the notable hardness of some thickened arteries, the “ whipcord ” or “ pipe-stem ” arteries, &c., examined clinically.

But how far is such feeling of abnormal resistance due to muscular contraction? And how is the amount of contraction and the concomitant resistance to compression to be gauged? We know that palpable arteries are often felt to be constricted, but this does not afford any measure of the relative intensity of such contraction as compared with the excised vessel in which the resistance has been experimentally determined, apart from the amount of guidance derivable from some considerations already advanced. If the arterial muscle is sufficiently active to keep the vessel at the size of the empty passive artery it is evident that the muscle is just counterbalancing the internal blood-pressure, and such degree of contraction can be correlated with the experimental results as regards resistance to compression. If the vessel is constricted (beyond the size of the passive empty tube) the muscular tone must be overbalancing the internal pressure and must have a higher value in resisting compression from without. With a high internal pressure an active condition of the arterial muscle may very appreciably exaggerate the systolic readings without causing any recognisable constriction of the tube, though of course if the artery is actually constricted against a high internal pressure the error introduced by the resistance of the wall will attain larger proportions, rising to higher numerical values the higher the readings are. When the readings are at all moderate and the vessel is not constricted we may conclude that the muscular tone cannot be playing any great part in exaggerating the indication of actual blood-pressure as expressed by the



obliteration readings. Of course it is only pronounced constriction that can be recognised clinically, the size of the passive tube (undistended by pressure) under various pathological conditions being unknown, varying much in different cases where the vessel may have become permanently dilated, *e.g.*, from long-standing high-pressure, deficient tone, &c.

But it is only up to a certain point that constriction of an artery runs parallel to increased resistance in its wall. When a certain small size of lumen is developed as a result of muscular contraction there may be no further change in the lumen, even though further change in the condition of the muscle may occur, involving a further increase of resistance to compression. In arteries like the brachial\* (normal and many pathological) the most powerful activity of the muscular coat fails to reduce the lumen below a certain small size, which may remain constant while a very considerable further increase in the resistance of the wall may occur. Consequently the amount of resistance associated with very marked constriction while always considerable is by no means constant.

On careful palpation an emptied artery (with the blood squeezed out or the brachial closed higher up) may feel quite soft; in that case it is plain that the wall resistance can play no important part in influencing the readings. If the artery feels hard there is not only the question of muscular contraction *versus* sclerosis, calcification, &c., but the further question as to whether the resistant character of the tube is continuous along such a length as is compressed by a 12 cm. armlet or is varied by one or more soft parts in its course; in the latter case the resistance of the greater part of the vessel would not influence the readings much, if at all, as the soft part would soon become closed as the compressing pressure mounts above the systolic internal pressure.

It is evident from the preceding statements that comparison of clinical arteries with excised by direct examination of the former is only capable of giving rough indications of a general nature, rather than precise results, the indications depending on (*a*) the presence or absence of a feeling of resistance in the emptied artery and (*b*) the presence or absence of constriction, with the distending influence of the blood-pressure acting on the vessel.

It is important to bear in mind that the condition of the radial artery is far from being a safe guide to that of the brachial, there being remarkable discrepancies between them in some cases. We have frequently found thickening and increased resistance to be much more pronounced in the brachial.

#### *Continued or repeated compressions.*

Our experiments with excised arteries have shown that in vessels offering considerable resistance to compression a notable lowering of the readings is induced by repeated compression or by keeping on the pressure

---

\* Exceptions have been found in some leg arteries from old and diseased horses and in somewhat smaller arteries from the legs of presumably healthy (young) oxen.

(general or local) for a few minutes. Manipulation and a massage of a contracted artery (by kneading or rolling between finger and thumb, &c.) causes striking relaxation; on keeping (in blood) for one or more hours contraction returns and the wall tube again gains firmness and resistance to compression. On the other hand repeated compression had no effect on the readings obtained from arteries showing nothing beyond a negligible resistance. The method thus serves as a means of detecting the presence of appreciable resistance in the arterial wall.

We were able to discriminate between altered conduction in the relaxed tube and an actual diminution in resistance to compression by using a continuous stream to perfuse the vessel in a very large number of experiments, having carefully correlated by other experiments the indications given by continuous and pulsatile streams respectively. With the continuous stream altered conduction of the systolic wave was not in question; the lowered readings could only have been due to diminished resistance of the arterial wall. Such diminution is so constant and characteristic as to constitute a valuable test for the presence or absence of pronounced resistance. A comparison of the points of disappearance and reappearance of the pulse, when a pulsatile stream is used, is also of assistance, at least if the obliterating pressure is kept on for some little time before the reappearance is tested. With a pulsatile stream local softening (by pressure) cuts down the obliteration reading in a remarkable way though conduction can hardly be altered thereby.

In view of the efficacy of these experimental methods of gauging the condition of the arterial wall and ascertaining whether it is offering resistance which would have to be deducted from the readings in order to get at the actual internal pressure, we have applied similar methods to human arteries under clinical conditions and have obtained very significant results, both of negative and positive character.

It is easy to demonstrate on a prominent temporal artery in a state of normal tone that external pressure (with the finger, &c.) repeated or continued for some time (*e.g.*, 2 min., &c.) causes decided relaxation limited to the compressed portion; the fall of blood-pressure beyond the compressed area does not induce any recognisable relaxation there. The effect is a direct one produced by the pressure acting on the arterial wall.

*Conduction of the systolic wave in changed conditions of the arterial wall.*

We cannot in this paper discuss the influence of arterial relaxation upon the conductance of the systolic wave, to which great importance has been ascribed by some investigators. Suffice it to say that we have investigated this point very fully, and in the light of our results find no ground for doubting that such influence is quite inconsiderable or practically negligible in connection with ordinary blood-pressure estimation by the obliteration method. We shall adduce our experimental evidence and discuss this subject elsewhere.



*Methods of repeated and continued compression.*

An armlet was placed on each arm and both were connected with a ball-filler or an Oliver's screw-compressor through a three-way tap by means of which they could be inflated simultaneously or in quick succession. The armlets were previously proved to give identical results on normal persons and when used on patients were interchanged from time to time, with no disturbance of the results in any case. After a synchronous estimation in the two arms, repeated compression was applied to one arm, the one giving the higher reading in cases of initial inequality, the pressure being let down to zero between each obliteration. Another synchronous estimation in both arms was then made to find the effects of repeated compression in one and to detect possible changes in general blood pressure by the reading from the other arm.

In some cases (as described later), where the vascular adjustments are ineffective or easily deranged, considerable disturbances of blood-pressure may be recognised during observations in which only one brachial is being closed. In cases showing any marked sensitiveness of this sort and in cases of slight hemiplegia, &c., we have avoided closing both brachials at the same time; the two arms were tested in such quick succession that there is little or no room for objection on that score.

In some cases groups of estimations were made from the arms alternately. In other cases the individual estimations were made alternately; in such series the readings often, though they may differ markedly in the two arms, may show a regularity in succession on each side, with or without a progressive change in level that quite excludes the idea of there being variations in general blood-pressure between the moment of estimation in one arm and the next in the other arm. In cases where the vascular balance is readily upset the obliteration test on one artery at a time is probably a more correct gauge of the pre-existing pressure than could be got by simultaneous constriction of the two limbs.

If the blood-pressure is liable to change extensively in the very brief interval between an estimation on one arm and a quickly succeeding one on the other arm (the apparatus being ready *in situ* with a suitable tap for permitting rapid alternation of the inflation of the two armlets) it would mean a variability which would make estimations of blood-pressure valueless, except as regards the indications afforded by the first reading with its possibilities of serious error.

Sometimes the armlets were placed on the forearms, or on arm and forearm; in the latter case estimations were made alternately in quick succession in the way already described for the two arms.

Instead of repeated compression by successive inflations of the armlet we have often employed digital compression of the brachial artery (for 2 or 3 min., &c.), near the middle of the region to be enclosed in the armlet; the armlet kept ready lower down the limb is then slipped into position and

at once inflated to test the obliteration point, as little time as possible being given for recovery of the artery from the digital compression.

Another method is to massage the artery, either with the vessel closed by digital compression higher up or without this.

The presence of unequal systoles introduces a complication in the examination of some cases. We have not relied on observations made on cases where marked inequality was present. We have always taken as the index the reappearance (or disappearance) of serial beats, not merely occasional ones. In very irregular pulses like that of auricular fibrillation no satisfactory estimation can be made.

### *Effects on normal arteries.*

*Arteries with normal tone.* Under the ordinary conditions of normal health repeated compression of the brachial or other artery used for blood-pressure estimation causes no appreciable difference in the readings even with as many as twelve or twenty re-compressions in succession. The differences between the disappearance and reappearance of the pulse are trivial when the tactile method is used and perhaps even less with the auditory method. These results support the view that the ordinary tone of the normal brachial artery presents no appreciable resistance to compression.

The same conclusion is in accordance with the results of the two experiments of Hill and Flack already mentioned in Part I. These experiments we have repeated with confirmatory results.

On the other hand apparently normal (*i.e.*, not recognisably thickened) arteries when hypertonically contracted give results similar to the positive results described when dealing with contracted and thickened arteries.

It is true that the application of heat to a limb (immersion for some time in hot water) may be followed by a somewhat lowered reading, which has been attributed to a softening of the arterial wall, affecting the blood-pressure reading by influencing the conduction of the systolic wave according to Hill, not by a changed resistance offered by the arterial wall.

But we do not feel warranted in interpreting the effects of heat as being solely dependent on any alteration which it may induce in the arterial wall, in view of the somewhat complex action of heat in causing relaxation of the peripheral vessels, modification of the pressure gradient in the limb, &c.

We do not find evidence in the observed effects of heating a limb to show that any appreciable resistance had been present in arterial wall prior to the application of heat.

The results obtained from different lines of investigation concur in showing that the normal brachial artery under ordinary conditions offers only a negligible resistance to compression.

*Arteries hypertonically contracted.* On the other hand apparently normal (*i.e.*, not recognisably thickened) arteries when hypertonically contracted



give results similar in their nature to the positive results described with reference to contracted and thickened arteries, though not necessarily identical as regards degree.

*Effects on thickened and contracted arteries.*

Hill,<sup>6</sup> with Flack and Holtzmann recorded lowered obliteration readings in some cases with thickened and tortuous arteries, &c., on repeated compression, the pressure being run up and down near the obliteration point. They attribute the effect not to diminution of arterial resistance to compression, the existence of which they do not believe in, but to relaxation of the vessel affecting the conduction (conductance) of the systolic wave, the wave being damped down in its passage along the relaxed vessel.

We use the term "thickened arteries" to include all the varieties in which this feature is present, whether characterised by "atheromatous" changes or by great thickening of the intima and often of the adventitia, or by increase of the media, the hypermyotrophy of Savill.

It must be borne in mind that an artery may be relatively inelastic towards internal pressure and may at the same time offer little resistance to compression from without.

*Negative results.* Our results indicate that many arteries with great thickening and defective elasticity show a quite unimportant resistance to compression with the armlet; this is in accordance with the great bulk of the evidence available from experiments on thickened arteries after excision, in conditions where there was no decided muscular contraction present.

In cases of this kind repeated compression induces in the readings no important reduction attributable to alteration in the compressed arterial wall and not to an actual lowering of the general blood-pressure. Similar readings were usually got from the two arms in such cases. Negative results of this kind are quite what might be expected in arteries with walls abnormally thick but not stiffened in the sense of being unusually resistant to compression, and in arteries with resistance unevenly distributed along the tube, interrupted in places by relatively soft and compressible portions. But it may also occur where the thickening seems to be a generalised change extending more uniformly along the tube. Failure to reduce excessively high readings may be seen both in cases with soft arteries and with greatly thickened and quite extraordinary tortuous ones.

*Positive results.* In many cases lowering of the readings in one arm from continued or repeated compression of that arm show a remarkable parallelism to what is seen in contracted excised arteries presenting marked resistance to compression. In the latter the internal pressure is known and the resistance of the arterial wall is evidenced by the difference between the internal and the external (obliteration) pressures. In clinical observations it is of course essential to ascertain from the other arm, whether a change of actual blood-pressure has occurred during the progress of recompression or

continued compression of the first arm. Not infrequently such may be the case; a later reading may be lower not from changed arterial resistance but from a reduction in general blood-pressure dependent on the passing off of slight excitement, &c., which may be present at the first reading, or on other causes. A reading from the other arm then gives the same lowered level the limb first tested gave on repeated compression.

But the obliteration readings may be reduced by continued or repeated compression apart from any evidence of concurrent lowering of the actual blood-pressure, a reduction comparable to the effect on excised contracted arteries under experimental conditions where possible changes in conductance were excluded. In both cases the lowering effects vary with the condition of the artery, the duration and intensity of the compression, the number of repetitions, &c. Again in regard to the partial or complete recovery with a rise in the readings, that occurs after an interval, the correspondence in results is very significant. And in both a similar variation is seen in the readiness with which arteries in different conditions yield to repeated compression, as shown by the lowering of their resistance.

The conclusion is obvious that local resistance can in certain cases play an important part in influencing and exaggerating blood-pressure readings under clinical conditions. We have advanced experimental evidence that this method does not discriminate between local resistance due to (a) muscular hypertonus or (b) to stiffening of the arterial wall due to other causes of such a sort as to offer much resistance to compression, if such occurs in the human body. So far as the available evidence goes there is no sufficient ground to warrant us in attaching much importance to the second factor (b). Contraction of a normal or hypertrophied media is the basis of the high resistance which we have found experimentally in normal or thickened arteries; when relaxation is induced (by warmth, &c.) even enormous resistances fall to small or even negligible amounts.

#### *Unequal readings from the two arms, etc.*

Very notable differences are sometimes found between the two arms, between arm and forearm, and between arm and leg. These differences are not necessarily constant; they may be found to alter markedly when examined at intervals of some days, or during the process of examination by repeated compression. The latter method commonly reduces the difference very markedly, if it does not remove it. In some instances the difference found in the two arms at the first reading on each occasion has been found to remain practically constant over long periods, many months, &c.

In many cases the differences are such as might, in the light of the results obtained with excised arteries be explained by the presence of a very unequal degree of contraction in the arteries examined. Of course the unequal readings are only a measure of the differences between the arteries on the two sides, not a measure of the total resistance on either side.



We do not discuss the question of differences in arm and leg pressures in this paper. Arm-leg differences of very large amounts have been described by Hill, Flack and Holtzmann after severe muscular exertion and in aortic regurgitation, and by Williamson in other conditions.

But we have sometimes met with such extensive variations (*e.g.*, 50-90 mm.) apparently due to local conditions on the two sides which can hardly be accounted for in the way indicated, unless we assume the occasional occurrence in morbid conditions of such enormous resistances as are sometimes seen (at room temperature, &c.) in excised arteries of old horses commonly showing very thick muscular coats or in such large and strong-walled vessels as the carotid of the ox. We have found (though rarely) arm differences so great as to be comparable to the arm-leg differences in obliteration values that have been described in aortic regurgitation.

It is of course important to bear in mind the hypermyotrophy described in human arteries by Savill,<sup>14</sup> Russell,<sup>13</sup> Dickenson and Rolleston<sup>1</sup> and others.

*Large variations in blood-pressure during repeated or continued compression.*

In employing repeated compression we have quickly let the pressure down to zero between each obliteration. We have used this plan rather than that (followed by Hill and Flack) of running the pressure up and down near the obliteration point, which does not differ as far as venous obstruction, sense of constriction, &c., are concerned from keeping on the pressure continuously. The last-named procedure causes, as has been noted by several observers, a certain rise of pressure (*e.g.*, 10-15 mm., &c.) in the normal person in a couple of minutes or so, and in some conditions of the circulation has in our experience had more extensively disturbing effects.

In rare instances repeated compression, as we have used it, has been accompanied by a large increase in the readings and apparently in the actual blood-pressure within a few minutes.

Even digital compression of the brachial artery, without constriction of the limb, has sometimes been attended by a very marked rise of pressure, as evidenced by the estimation of systolic or diastolic pressure in the other limb or even by the finger on the radial artery. This rise of pressure may outlast the period of compression for some time.

This is in marked contrast to what happens under similar circumstances in the normal individual, in whom we have found no change of reading from one arm as a result of closure of the other brachial. No doubt the difference depends on the presence, in the cases referred to, of a defective functioning of the normal mechanism which compensates for the alteration in peripheral resistance involved in the closure of an artery like the brachial. Important information as to the balanced working of the vascular adjustments may be gained by such observations in different conditions.

In regard to this rise of pressure, it is to be noted that here we are dealing with a change of which there is no parallel in the results obtained with excised surviving arteries; in the latter the change, if any, is always a lowering of the obliteration readings, never a rise. When heightened readings are got in man the alteration depends, as far as we have seen, on a rise of general blood-pressure, which can be recognised by examining other limbs, &c. This rise is as a rule mainly, if not wholly, dependent on changed peripheral resistance; the rate of the heart beat may remain unchanged or it may be somewhat slowed. The diastolic readings are raised as well as the systolic.

It is evident that in some such cases the obliteration readings may be strikingly different in the same patient at the same time according to the limb or segment of limb examined, and the takings of first readings or later ones after several recompressions; in the last instance the change may be either to a higher or a lower level according as to whether changes in general blood-pressure or effects on the arterial wall predominate, the latter being in our experience by far the more common.

In attempting to apply the ingenious method, used by Hill and Flack, of comparing the height to which the venous pressure in the forearm can rise when the compression applied to the arm is a little below arterial systolic pressure, we have experienced much difficulty, and have not obtained any definite results in pathological cases where the blood-pressure is liable to vary much on account of the discomfort caused by the continued constriction of the arm and the disturbance of the general blood-pressure induced, the arterial pressure rising while the venous pressure is being estimated, &c..

The sensitiveness of sclerosed vessels, or rather of the vascular system, as shown by the occurrence of more or less extensive (slow) changes in blood-pressure from relatively small causes has been commented on by many observers.

When we first noticed a difference of as much as 60 mm. at the first reading within forty-eight hours in a patient (old) whose general condition showed no apparent alteration, we were disposed to suspect some fallacy, but soon we had opportunities of witnessing equally large variations within the period of examination by a series of repeated compressions, &c.

It is true that the foregoing results have been obtained from old patients with far-reaching defects of the balanced mechanisms of the vascular mechanism on which its normal smooth working depends. But is there any warrant for assuming that similar derangements may not be present at much earlier ages under the varied conditions of disease?

*Classification of the effects of continued or repeated compression.*

The effects of continued or repeated compression applied clinically fall into the following categories:—

(1) In the generality of cases, when no abnormality of the vascular mechanism is present the result is practically nil, excepting that in some



persons there may be a decided reduction of the obliteration reading not dependent on an alteration in the resistance of the arterial wall but due to the passing off of slight alarm, excitement, &c., which may be present at the first reading. That such is the cause of the reduction is indicated by a reading from the other limb, in which the first reading gives the same lowered level as is found in the first limb after repeated compression.

(2) Similar negative results are obtained in many cases of arterial disease where the thickening is of an uneven or patchy character or associated with atrophic changes in the media and hypertrophy of the intima, atheroma, &c., or where the hypertonus is unevenly distributed, as is often seen in excised arteries. When high readings are obtained, not appreciably lowered by repeated compression, the diastolic readings are also frequently high, though by no means always, in the absence of abnormally slow heart-beat, aortic regurgitation, &c.

Excessively high readings not reduced by the method in question are found both with soft arteries not recognisably thickened and also with thickened and extremely tortuous ones that feel resistant to the finger.\*

(3) In many cases where an abnormal resistance is presented by the arterial wall from muscular contraction, with or without thickening of the media, repeated compression produces a marked lowering of the readings, essentially due to a diminution of the resistance, though it may at times be associated with some lowering of the general blood-pressure, as indicated by examination of the other arm, &c. Such reduction is a valuable indication of the presence of abnormal resistance in the arterial wall, a factor which makes the initial reading yield an exaggerated estimate of the actual blood-pressure within the vessel. A very high initial reading falling on repeated compression to a moderate level is commonly associated with a moderate diastolic pressure, excessively small in proportion to the initial (exaggerated) systolic reading.

The reduction may be very unequally manifested in different limbs or segments of limbs.

(4) In some cases with abnormal instability of the vascular mechanism a more or less extensive rise in the readings occurs, depending, mainly at least, on a rise in the actual blood-pressure.

Such rise in general blood-pressure may more or less completely conceal or may quite overbear the effect of any reducing influence exercised upon the resistance of the wall of the compressed artery.

---

\* Marked tortuosity means that the arterial tone, which resists elongation as well as transverse expansion, has been deficient either absolutely or relatively to the internal pressure. An artery with deficient tone may elongate and become tortuous with normal internal pressure, while another even with increased tone may after a time yield to excessive internal pressure. Some extremely tortuous arteries are very possibly beyond the phase of resistance to compression, if they have ever passed through such a phase.

*First and subsequent readings.*

As regards first readings of the blood-pressure by the obliteration method the following conclusions have been arrived at.

In cases with normal arteries or pathological arteries presenting no appreciable or important resistance to compression, the first reading, whether disappearance or (preferably) reappearance of the pulse is taken as the index, is approximately correct as an indication of the actual systolic pressure. The actual pressure may, however, be influenced by excitement, &c., at the first reading.

When there is marked resistance in the arterial wall a first reading may give very seriously erroneous values both in regard to disappearance and reappearance of the pulse, the error with the latter index being decidedly less than with the former. Repeated compression greatly reduces or rectifies this error in many cases. The number of re-compressions necessary to do this varies greatly.

But in some instances the process of repeated compression introduces a fresh complication by exciting a rise of general blood-pressure. Thus the means taken to correct the first source of error introduces a second factor which disturbs the estimation in the opposite direction from the first.

While it may be possible by repeated compression to minimise or practically eliminate the resistance of the arterial wall so as to render practicable a determination of the actual pressure then obtaining within the artery, this latter pressure is at the new level to which it has been raised during the repetition of the compression in the special cases referred to.

In such cases it would seem to be impracticable to arrive, by the ordinary obliteration method, at an accurate estimate of the actual blood-pressure as it was before the process of estimation was commenced.

*Some illustrative cases of different types.**CASE 1.*

M. T., *aet.* 74. Brachials tortuous and resistant; much more so than radials. Pulse rate 90; second aortic sound greatly accentuated. Synchronous estimations in the two arms.

D.—disappearance, and R.—reappearance of pulse.

|    |    |    | RIGHT. | LEFT. |
|----|----|----|--------|-------|
| R. | .. | .. | 240    | 240   |

Left brachial closed by digital compression at middle of arm for three minutes. Arms tested again.

|    |    |    | RIGHT. | LEFT. |
|----|----|----|--------|-------|
| D. | .. | .. | 244    | 244   |
| R. | .. | .. | 240    | 238   |

In this case the disappearance and the reappearance were simultaneous in the two arms, and this remained unaffected by the digital closure of one brachial; the equality in the two arms persisted. The actual pressure was evidently an excessively high one, there being no evidence that the arterial wall influenced the readings appreciably.

To the finger the pulse felt a very incompressible one.



## CASE 2.

M. Y., *aet.* 68. Pulse 76. Arteries thick and resistant after brachials closed high up, especially on left side. Synchronous estimations in arms.

|    |    |    | LEFT. | RIGHT.                                  |
|----|----|----|-------|---|
| R. | .. | .. | 220   | 190                                     |
|    |    |    |       | Left brachial closed for three minutes. |
| D. | .. | .. | 204   | 204                                     |
| R. | .. | .. | 196   | 196                                     |

Here the difference of 30 mm. between the two arms gave place to equality after continued compression of the artery on the side giving the higher reading.

## CASE 3.

M.D., *aet.* 74. Pulse 126. Synchronous examination of arms.

|    |    |    | LEFT. | RIGHT.                                   |
|----|----|----|-------|--|
| R. | .. | .. | 205   | 240                                      |
|    |    |    |       | Right brachial closed for three minutes. |
| R. | .. | .. | 225   | 225                                      |

Here an arm difference of 35 mm. was changed to equality, with apparently something of a rise (about 20 mm.) of actual pressure, as a result of continued compression of the artery giving the higher reading at the first estimation.

## CASE 4.

J.S., *aet.* 68. Arteries thickened.

Repeated compression was employed with lowering effects on the readings strikingly similar to those seen on similar compression of an excised artery in tonic contraction.

| OBS. |    |    | LEFT ARM. |
|------|----|----|-----------|
| 1.   | .. | .. | D. 184    |
|      |    |    | R. 178    |
| 2.   | .. | .. | D. 179    |
|      |    |    | R. 170    |
| 3.   | .. | .. | D. 174    |
|      |    |    | R. 165    |
| 4.   | .. | .. | D. 170    |
|      |    |    | R. 162    |
| 5.   | .. | .. | D. 164    |
|      |    |    | R. 159    |
| 6.   | .. | .. | D. 164    |
|      |    |    | R. 160    |

The right arm was then tested immediately.

| OBS. |    |    | RIGHT ARM. |
|------|----|----|------------|
| 1.   | .. | .. | D. 187     |
|      |    |    | R. 178     |
| 2.   | .. | .. | D. 182     |
|      |    |    | R. 174     |
| 3.   | .. | .. | D. 170     |
|      |    |    | R. 166     |
| 4.   | .. | .. | D. 164     |
|      |    |    | R. 160     |
| 5.   | .. | .. | D. 161     |
|      |    |    | R. 158     |
| 6.   | .. | .. | D. 160     |
|      |    |    | R. 157     |
| 7.   | .. | .. | D. 162     |
|      |    |    | R. 158     |

It is clear that in this case the actual blood-pressure was not above 158, though the first readings were 20 mm. higher. That the gradual reduction

in the values obtained from the first arm were not due to a gradual lowering of the actual blood-pressure is evidenced by the fact that the second arm, tested at once, gave to begin with as high a reading as the first arm had done ; then came a similar gradual decline.

### CASE 5.

A.C., *act.* 81. Pulse rate 56. (December the 18th, 1912.) Readings taken alternately from the two arms (see numbering).

| RIGHT ARM. |     |     | LEFT ARM. |     |     |
|------------|-----|-----|-----------|-----|-----|
|            | D.  | R.  |           | D.  | R.  |
| (2)        | 220 | 210 | (1)       | 140 | 135 |
| (4)        | 225 | —   | (3)       | 150 | 140 |
| (6)        | 200 | 190 | (5)       | 140 | 135 |
| (8)        | 200 | 195 | (7)       | 140 | 135 |
| (9)        | 200 | 195 |           |     |     |

R. Brachial artery compressed for three minutes.

|      |     |     |
|------|-----|-----|
| (10) | 180 | 175 |
| (11) | 180 | —   |

Fall of 40 mm. in R. arm (after trivial preliminary rise) follows repeated compression.

In L. arm, slight preliminary rise, then no change ; compression not repeated very often.

The inference from these observations is that the actual blood-pressure is not over 135 mm.

The same case on January the 13th, 1913. Pulse rate 54.

| RIGHT ARM. |     |     | LEFT ARM. |     |     |
|------------|-----|-----|-----------|-----|-----|
|            | D.  | R.  |           | D.  | R.  |
| (2)        | 230 | 220 | (1)       | 135 | 130 |

*Armlets put on forearms.* (Each armlet kept on same side as in preceding observation.)

| RIGHT FOREARM. |     |     | LEFT FOREARM. |     |     |
|----------------|-----|-----|---------------|-----|-----|
|                | D.  | R.  |               | D.  | R.  |
| (4)            | 260 | 255 | (3)           | 200 | 195 |

*Armlets on upper arms.* Armlet from right arm (which had given high pressure) now put on left upper arm and *vice versa*.

| RIGHT ARM. |     |     | LEFT ARM. |     |     |
|------------|-----|-----|-----------|-----|-----|
|            | D.  | R.  |           | D.  | R.  |
| (6)        | 280 | 270 | (5)       | 185 | 180 |

*Armlets on forearms.*

| RIGHT FOREARM. |     |     | LEFT FOREARM. |     |     |
|----------------|-----|-----|---------------|-----|-----|
|                | D.  | R.  |               | D.  | R.  |
| (7)            | 210 | 200 | (8)           | 170 | 165 |
|                | 215 | 210 |               | 175 | —   |
|                |     |     |               | 155 | 150 |

These observations show several noteworthy features.

(1) The extraordinary initial difference between the two arms, 95 mm. when tested by the disappearance and 90 mm. by the reappearance of the pulse.

(2) The remarkable rise of pressure (50 mm.) which occurred while the estimations were being made. That such was a true rise of pressure is shown by the exact parallelism in the alteration of the readings shown in observations (5) and (6), the differences between the two arms being still 95 (D) and 90 (R) at the new (elevated) level.



(3) The difference between the forearms (40-60 mm.) is not the same as the arm difference.

The same case on January the 14th, 1913.

*Armlets on left upper arm and forearm.*

|                    |    |    |    |        |
|--------------------|----|----|----|--------|
| (1) Left forearm   | .. | .. | .. | 162 D. |
|                    |    |    |    | 158 R. |
| (2) Left upper arm | .. | .. |    | 154 D. |
|                    |    |    |    | 152 R. |
| (3) Left upper arm | .. | .. |    | 152 D. |
|                    |    |    |    | 150 R. |
| (4) Left forearm   | .. | .. | .. | 164 D. |
|                    |    |    |    | 158 R. |

*Armlet shifted from left forearm to right upper arm.*

|               |    |    |    |        |
|---------------|----|----|----|--------|
| (5) Right arm | .. | .. | .. | 250 D. |
|               |    |    |    | 246 R. |
| (6) Left arm  | .. | .. | .. | 156 D. |
|               |    |    |    | 154 R. |

*Armlet on right thigh. Popliteal felt.*

|        |
|--------|
| 190 D. |
| 185 R. |
| 190 D. |
| 185 R. |

(On January the 31st, 1913, the systolic reading from the right arm was 248 mm.)

The extraordinary difference between the two arms in this case suggested the question of there being some structural peculiarity in the vascular channel of the left limb, *e.g.*, partial obstruction, &c., which might cut down the systolic wave in that limb. The fact of the radial pulse being quite as good on the left side did not support such a hypothesis, but it was not conclusive, for the right radial artery might be the seat of structural change which prevented it giving a fair representation of the systolic wave in the right brachial. Still the fact of there being a good systolic wave in the left radial was significant. Still more significant is the obtaining of a somewhat higher reading from the left forearm than the left arm. It need hardly be said that the blood-pressure is not likely to be higher in the forearm than in the arm; the excess shown by the reading represents an exaggeration due to local conditions, the state of the arterial wall, &c. This of course strongly favours the view that the exceedingly high reading in the right arm is similarly an exaggeration. Further support is lent to this view by the fact that the diastolic pressure estimated in the right arm is quite an ordinary one (80 mm.), such as might be expected from the systolic reading in the left arm (135 mm.). The absence of any accentuation of the second aortic sound militates strongly against the idea of the actual pressure in the aorta being anything like so high as the right arm readings. Neither radial pulse is at all difficult of compression, the right somewhat less so than the left, a striking difference from the arm readings. That the very high reading in the right arm is an exaggerated one is indicated by the very marked lowering (40 mm.) which followed repeated compression while the pressure reading (probably true blood-pressure) in the left arm remained unaltered. Of course there still remains a large excess, after the reduction of 40 mm., in the right arm to be accounted for, the total excess being such as we have

only seen in excised arteries in conditions of enormous contraction at room temperature, &c., conditions very remote from those obtaining in the human body. To what extent the right arm difference might yield to further compression, &c., we are not prepared to say. The reduction induced by compression is very completely recovered from; the next day the patient was examined and the readings were found to be at the initial level. Indeed in this case the readings have shown notable constancy on the various occasions when they were taken, extending over the greater part of a year.

There was no evidence of error being introduced into the readings by contraction of the arm muscles. In addition to direct examination to detect this source of fallacy, the remarkable constancy of the first readings is against the idea of so variable a disturbance as would be likely to result from skeletal muscular contraction. No sign of such contraction was observable during the use of an Erlanger apparatus, with which indications of muscular contraction occurring during the observations are readily discernible.

In this case it would clearly be impossible to account for the difference between the arms on the assumption that a rigid artery on the right side transmitted the systolic wave from the aorta almost unimpaired in height, while a soft artery on the left side damped it down very greatly. Such an assumption would imply that the aortic pressure was truly indicated by the right arm reading while there was an enormous loss on the left side, between the aorta and the brachial. There is evidence, derived from various sources, to show that such a loss is out of the question. Further, if an immense loss occurred between aorta and brachial there ought to be much further loss between arm and forearm, unless the conditions in that part of the limb were entirely different. But instead of being much lower the forearm reading was actually higher than the arm reading, a fact inexplicable on the conduction hypothesis. Again, the marked lowering (40 mm. on one occasion; 60 mm. on another, &c.) induced by digital compression in the right arm (without change in the left) could not be explained by altered conductance depending on relaxation of the vessel, for the compression was confined to one spot, pressed on by the tips of two fingers with rapid intermissions—a local massage.

### CASE 6.

M.G., *act.* 77. Alternate series of estimations made on the two arms.

The order in which the limbs were examined is indicated by the letters A, B, &c., the serial observations on each limb by the numerals.

#### A. LEFT ARM.

|     |     |
|-----|-----|
| (1) | 200 |
| (2) | 200 |
| (3) | 170 |
| (4) | 160 |
| (5) | 165 |
| (6) | 155 |
| (7) | 152 |

#### B. RIGHT ARM.

|     |     |
|-----|-----|
| (1) | 175 |
| (2) | 175 |
| (3) | 170 |
| (4) | 175 |

#### C. LEFT ARM.

152

#### D. RIGHT ARM.

Brachial artery compressed for two minutes.

|     |     |
|-----|-----|
| (1) | 150 |
| (2) | 155 |
| (3) | 160 |
| (4) | 155 |

In this case the actual blood-pressure was evidently not over 152. The two arms giving different readings to begin with came to give practically



the same readings in the end, both falling to about the same point from the initial unequal levels. The fall in the left arm from 200 to 152 might of course be partly due to a fall of actual blood-pressure. That it was by no means wholly, if at all, due to such is shown by the reading of 175 got from the right arm immediately after the 152 in the left; the pressure in the right kept up to about 175, and then the left was found to be still at the same lower level as before. Digital compression of the right brachial was followed by a lowering to practically the same level as the left. At intervals of a few weeks in this case variable first readings were got, 140, 138 and 180, without evident change in the general condition.

### CASE 7.

*M.B., Act. 74.* Pulse rate 70. Arteries very firm and tortuous; generalised thickening.

#### A. RIGHT ARM.

- (1) 240
- (2) 230
- (3) 240-245
- (4) 250
- (5) 270-280

#### B. LEFT ARM.

- (1) 270
- (2) 250
- (3) 235
- (4) 230
- (5) 220
- (6) 215
- (7) 215

#### C. RIGHT ARM.

- (1) 240
- (2) 260
- (3) 260-265
- (4) 250

#### D. LEFT ARM.

- (1) 230
- (2) 210
- (3) 215
- (4) 215

Here the remarkable results are evident inasmuch as repeated compression of the right arm gives a rise in the readings while repeated compression of the left gives a progressive lowering. In the case of the right the compression evidently causes a rise of general blood-pressure, the left arm giving a similar high reading immediately after the first series (A). The fall from 270 to 215 in series B is apparently due partly to diminished arterial resistance and partly to an actual fall of blood-pressure, as indicated by the reading of 240 got immediately after from the right arm. Again on repeated compression a rise of about 15 occurs in the right arm C, which shows by a rise of 15 in the left arm at the beginning of D, as compared with the end of series B, though the reading is still lower than on the right side. The interpretation we put upon these results is that the actual blood-pressure is not above 215, and that the higher reading in the right arm is due to excess of resistance on that side. The variation of the readings seems to be due partly to actual changes in the blood-pressure and partly to alterations in the resistance of the arterial wall during the repeated compressions. It is obvious that by taking the verdict of the obliteration tests at different points in the series of estimations, the estimate of "blood-pressure" might be anything from 210 to 270-280.

It should be added that this was the only case in which so striking a difference in the nature of the results obtained from the two arms was observed.

The same patient as in *CASE 7* six weeks afterwards. Pulse rate 70.

| LEFT ARM.   |     |     | RIGHT ARM. |     |     |   |
|---|-----|-----|------------|-----|-----|---|
|   | D.  | R.  |            | D.  | R.  |   |
| (1)   | 145 | 140 | (2)        | 185 | 180 | Compression kept on for<br>a little time. |
| (3)   | 145 | 140 |            | 195 | 190 |   |
|   | 165 | 160 | (4)        | 170 | 160 |   |
| (5)   | 160 | 155 | (6)        | 130 | 125 |   |
| (7)   | 130 | 125 | (8)        | 120 | 115 |   |
| The diastolic reading at the end of the series was 80 mm. |     |     |            |     |     |   |

The diastolic reading at the end of the series was 80 mm.

Here there was an initial difference of 40 mm. between the two arms, coming down on repeated compression to within 10 mm., a fall of 15 mm. in the left arm and of 65 mm. in the right arm, showing that the readings were affected in a very important way by the local conditions in the arms, a change in the general blood-pressure being obviously not an adequate explanation. The actual pressure was evidently not over 115 mm. while the initial reading in the right arm had been 180 mm. (R). It is possible that the actual blood-pressure may have fallen slightly, but if so, the fall was in all probability not more than was indicated in the readings from the left arm, which would leave an error of 50 mm. in the right arm.

Another point to be noticed in this case is the readiness with which the blood-pressure rose when the compression was kept on the limb, the effect of the latter speedily masking or overbearing the lowering effect of repeated compression. This illustrates the interplay of two factors, (*a*) the disturbing influence on the general balance of the vascular mechanism, and (*b*) the local effect on the artery diminishing the resistance of its wall.

To put to a further test the effect of continued compression, digital compression of the right brachial artery (without constriction of the limb) was tried for two minutes, while an armlet was still left on the left arm. It was found that both systolic and diastolic pressures were raised, the former from 125 to 175, and the latter from 90 to 105.\* The respiration was accelerated and deepened and there were general signs of restlessness. The pulse was slightly slowed from 66 to 62-63. That there was a rise of blood-pressure was easily recognisable by the finger on the radial artery, the alteration in compressibility being very notable. It need hardly be remarked that in such a case as this simultaneous closure of both brachials, in order to get synchronous readings, would not be a feasible procedure.

## CONCLUSIONS (PART II).

(*The conclusions for Part I are given on page 299.*)

Estimations of systolic blood-pressure by the obliteration method, when made with suitable precautions, give substantially correct results in ordinary conditions of normal health and also in the great majority of cases

---

\* The diastolic pressure was tested both during and after the digital compression; the systolic not till the right brachial had been released from digital compression. The rise in both pressures was found to persist for some time afterwards.



of illness in the collective sense. Even when the disease affects the vascular system with thickened arteries, &c., the indications are in the majority of cases approximately correct, the readings ranging from moderate or low to very high values. It is only in a minority of cases that any serious error is liable to occur, in the direction of over-estimation.

In some such cases the influences of local conditions may be very important, especially the presence of abnormal resistance in the arterial wall, depending mainly at least on contraction of the muscular coat. In such conditions very different readings may be obtained from the same person on the same occasion according to the limbs or parts of limbs examined, the using of first or later readings, &c.

Continued or repeated compression, with comparison of the two sides, &c., affords a valuable method of detecting the presence of such error, though not invariably decisive. In some instances considerable disturbances of blood-pressure may occur. Results, both positive and negative, obtained by this method show a striking parallelism to those yielded by excised surviving arteries.

Remarkable variations of blood-pressure may occur in some cases with no very evident change in the general condition of the patient.

We have to record our thanks to Dr. G. Spencer Melvin for valuable assistance in the later part of our inquiry, on both the experimental and the clinical sides, and we have to express our indebtedness to Dr. Clifford Bell for selecting and enabling us to examine a series of highly suitable cases.

#### BIBLIOGRAPHY.

- <sup>1</sup> DICKENSON AND ROLLESTON. *Lancet*, 1895, II, 137.
- <sup>2</sup> HENSEN. *Deutsch. Archiv. f. klin. Med.*, 1900, LXVII, 443.
- <sup>3</sup> HERRINGHAM. *Proc. roy. Soc. Med. (Med. Sect.)*, 1908-9, II, 37.
- <sup>4</sup> HILL. "Further Advances in Physiology," 1909, 126.
- <sup>5</sup> HILL AND FLACK. *Brit. med. Journ.*, 1909, I, 272; *Proc. physiol. Soc.*, XLVIII, *Journ. of Physiol.*, 1909, XXXVIII.
- <sup>6</sup> HILL, FLACK AND HOLTZMANN. *Heart*, 1909, I, 73.
- <sup>7</sup> JANEWAY AND PARK. *Archives of internal Med.*, 1910, VI, 586.
- <sup>8</sup> MARTIN (C. J.). *Brit. med. Journ.*, 1905, I, 865.
- <sup>9</sup> MULLER AND BLAUDEL. *Deutsch. Archiv. f. klin. Med.*, 1907, XCI, 517.
- <sup>10</sup> MUMMERY. *Proc. physiol. Soc.*, XXIII, *Journ. of Physiol.*, 1905, XXXII.
- <sup>11</sup> OLIVER. "Studies in Blood-Pressure" (2nd edit.), 1908, 111.
- <sup>12</sup> RUSSELL. "Arterial Hypertonus, Sclerosis and Blood Pressure," 1908, 87.
- <sup>13</sup> RUSSELL. *Brit. med. Journ.*, 1912, I, 659.

- <sup>14</sup> SAVILL. Trans. pathol. Soc., 1904, LV, 375; Brit. med. Journ., 1897, I, 188.
- <sup>15</sup> SCHMIDT. Arch. f. Anat. u. Physiol., 1909, Physiol. Abth., 331.
- <sup>16</sup> SCHOLTYSSEK. Archiv. f. Anat. u. Physiol., 1909, Physiol. Abth., 323.
- <sup>17</sup> VOLHARD. Verhandl. d. Kongress f. innere Med., 1909, XXVI, 200.
- <sup>18</sup> VON BASCH. Zeitschr. f. klin. Med., 1880, II, 6; Berl. klin. Wochenschr., 1887, XXIV 181.
- <sup>19</sup> WILLIAMSON. Proc. roy. Soc. Med. (Med. Sect.), 1908 9, II, 229.



# THE EXCITING CAUSES OF VENTRICULAR FIBRILLATION IN ANIMALS UNDER CHLOROFORM ANÆSTHESIA.

By A. GOODMAN LEVY.

(From the Research Laboratories of the Medical School, University College Hospital.\*)

## CONTENTS.

|  | PAGE. |
|--|-------|
| <i>Introduction—</i>   |       |
| <i>Retrospect</i> .. .. .  | 320   |
| <i>Methods of experiment</i> .. .. .   | 321   |
| <i>Definitions</i> .. .. .   | 324   |
| <i>Types of irregularities</i> .. .. .   | 324   |
| <i>Recovery from ventricular fibrillation</i> .. .. .  | 324   |
| <i>I. The direct cardiac effect of adrenalin—</i>  |       |
| (a) <i>general aspects of the reaction</i> .. .. .   | 325   |
| (b) <i>control experiments</i> .. .. .   | 328   |
| (c) <i>the cardiac action of adrenalin</i> .. .. .   | 330   |
| (d) <i>the reaction in chloroformed dogs</i> .. .. .   | 331   |
| (e) <i>the reaction in the chloroformed human subject</i> .. .. .                                  | 331   |
| <i>II. The direct cardiac effect of excitation of the accelerator nerves</i> .. .. .               | 333   |
| <i>III. The reflex cardiac effect of sensory excitation</i> .. .. .                                | 336   |
| (a) <i>The paths of action of sensory reflexes</i> .. .. .   | 341   |
| (b) <i>Reflex cardiac syncope in the chloroformed human subject</i> .. .. .                        | 346   |
| <i>IV. The direct cardiac effect of section of the vagi</i> .. .. .                                | 348   |
| <i>V. Ventricular fibrillation of apparently spontaneous origin—</i> .. .. .                       |       |
| (a) <i>observations without recording apparatus</i> .. .. .  | 353   |
| (b) <i>observations with recording apparatus</i> .. .. .   | 361   |
| (c) <i>death in man during the induction and recovery periods of chloroform anæsthesia</i> .. .. . | 369   |
| <i>Discussion</i> .. .. .  | 371   |
| <i>General conclusions</i> .. .. .   | 376   |
| <i>Bibliography</i> .. .. .  | 376   |
| <i>Appendix</i> .. .. .  | 377   |

\*A part of the expenses of this research was defrayed by a grant made by the Graham Research Fund, University of London.

## INTRODUCTION.

*Retrospect.*

A SERIES of cases of sudden death in animals under the influence of chloroform was alluded to in a preliminary communication<sup>14</sup> to the Physiological Society about two years ago, and it was therein shown that these deaths were due to fibrillation of the ventricles. In a later communication<sup>15</sup> I described in detail the manner of death occurring during the stage of the induction of chloroform anæsthesia, and it was shown that in these cases likewise the ventricles fibrillated.

I have now succeeded in producing this cardiac phenomenon by a number of experimental methods.

The key to the solution of the problem was afforded by observations upon *cardiac irregularities* which developed spontaneously in cats when the strength of the chloroform was diminished, or on cessation of administration, these irregularities frequently assuming a form which was identical with that which was likewise observed to be an invariable antecedent to the act of fibrillation. Further light was afforded by the observation that small quantities of adrenalin injected into the blood of the lightly chloroformed animal caused ventricular fibrillation, an action likewise described in the afore-mentioned preliminary communication.

These observations were confirmed and their relationship expounded in an investigation undertaken in conjunction with Dr. T. Lewis<sup>21</sup> into the electro-cardiographic phenomena of chloroformed cats. The irregularities were therein recognised as the result of premature contractions (or extrasystoles) arising from various foci in the ventricles and exhibiting grades of complexity ranging from single extrasystoles arising in a single abnormal point up to a rapid succession of extrasystoles from several different foci (multiple tachycardia). When the ventricles exhibit these latter complicated irregularities, they are in a state of potential fibrillation, fibrillation being but a progressive stage in the chain of events.

It is evident in studying ventricular fibrillation that great importance must be attached to the observation of these irregularities as constituting antecedent stages, and as affording minor evidences of a process which, in a more intense form, would terminate in complete cardiac syncope. The conclusions of other investigators regarding the source of origin of these irregularities have therefore suggested the lines of investigation that I have adopted in tracing out the exciting causes of ventricular fibrillation.

There are two main theories extant relating to the production of ventricular abnormalities in hearts held to be acting under normal conditions : (1) that supported by Hering,<sup>9</sup> Knoll,<sup>13</sup> and Heidenhain,<sup>8</sup> which refers their production to an increase in the intracardiac tension, further supported by MacWilliam's view<sup>22</sup> that ventricular fibrillation is purely mechanical in origin ; (2) that supported by Rothberger and Winterberg<sup>25</sup> and by Garrey,<sup>6</sup> which refers their production to nervous influences.



The theoretical considerations thus briefly indicated are in many respects complicated and obscure, but it is evident that either or both of these two views may be held to afford an interpretation of the adrenalin reactions. Adrenalin, as is well known, is held to act upon the myoneural junctions of the entire sympathetic distribution, thus stimulating the heart in addition to producing a general vasoconstriction, and hence this research in taking the adrenalin reaction as a starting point, has branched off into two well-defined paths. From this paper, however, with the exception of one important reference, I am excluding the whole of the details of my work relating to the pressor influences under chloroform, for although at the beginning I favoured a theory of reaction to a raised intracardiac tension and found much apparent confirmation of it, it became evident that many of the pressor influences were associated with cardiac augmentor influences, and ultimately I failed to find definite evidence that pressor changes bore any relation of importance to the production of these described cardiac irregularities under chloroform. That portion of the work will be therefore more conveniently considered later in a separate paper.

On the other hand by pursuing the alternative theory of a direct cardiac action, I have been led to constant and coherent results which are open to a definite theoretical interpretation, although this interpretation is not that of the production of the irregularities through influences which are *necessarily* of a nervous character, as will appear in the course of this paper. The conclusions at which I have thus arrived have such an important practical reference that I have felt constrained to embody in this paper the essential features of my research whilst certain theoretical points remain under consideration, leaving the detailed account of many of my earlier experiments to be considered in a following paper.

I have pleasure in here expressing my indebtedness to Dr. T. R. Elliott and Dr. T. Lewis for the assistance I have received from them in following up my subject; the special knowledge which each possesses has been very helpful in many respects.

### *Methods of experiment.*

All the experiments herein described were performed upon cats. The blood-pressure curves were registered from an artery, generally the carotid, by means of a Ludwig's mercury manometer or a Hürtle's membrane manometer, employed independently, or, as in some cases, conjointly according to a method described by Sollman and Pilcher,<sup>28</sup> of damping the mercurial oscillations down to their smallest dimensions by means of a screw clamp on the rubber connecting tube, so that a quantitative indication only of the mean blood-pressure is inscribed without affecting the more delicate record of the individual heart beats traced simultaneously by the lever of the membrane manometer. A typical example of such a combined curve is shown in Fig. 6.



The mercury manometer, when used alone, affords a very graphic representation of fluctuations of blood-pressure and cardiac pauses and is therefore the most ready means of recognising the onset of irregularities, but it is liable to slur over, or totally obscure the individual abnormal beats, and it is for the proper analysis of these that the Hürtle manometer is found useful. This latter instrument has however the disadvantage of occasionally rendering the more extreme degrees of irregularities (multiple tachycardias) as an apparently regular, or almost regular sequence. The two forms of record thus reciprocate, and their respective features are illustrated in the curves reproduced in Fig. 1, *a*, *b* and *c*.

A half saturated solution of sodium sulphate was employed to fill the manometer and its connecting tubes.

The chloroform vapour was administered by passing it, mixed with air in suitable proportions, through the small end of a funnel which covered the head of the animal (the so-called *ad plenum* method of administration). The percentage of vapour was regulated by means of an appliance elsewhere described<sup>17</sup>; this was attached to the inlet pipe of a Brodie's pump, a distended rubber bag on the delivery tube of the latter serving to convert the intermittent into a continuous stream.\* The animals were anæsthetised by submitting them from the start to the influence of a 2% vapour, which was continued without intermission; the percentage being ultimately increased sufficiently to produce complete muscular relaxation.

In order to perform control experiments upon a cat not affected by any anæsthetic, and also in order to study the induction of chloroform anæsthesia from the first moment of the administration, two methods were adopted. (1) That described by Brooks<sup>2</sup> whereby an artery was prepared under a general anæsthetic one day, and on the next a cannula was slipped into it without difficulty under a local anæsthetic only. In some cases I employed the special form of metal cannula described by Brooks. (2) The cat was rendered anæsthetic by passing a stylet into the foramen magnum and cutting across the *crura cerebri*. Sometimes it was possible to avoid injury to the bulb and then natural respiration was maintained, otherwise artificial respiration was carried out in these cases. In both of these two methods chloroform narcosis could be subsequently induced in the usual manner.

The successful demonstration of the results hereinafter described depends essentially upon a precise control of the anæsthetic—this degree of anæsthesia must, on the one hand, suffice to obviate the supervention of spontaneous irregularities, and on the other hand be insufficient to depress the heart to the point of modifying or preventing the onset of these irregularities when an attempt is made to excite them, or to depress the reflex mechanisms involved in some of the experiments. For these reasons prolonged dissections or severe operations are inadvisable, and negative

---

\*For purposes of artificial respiration the bag was discarded, and the intermittent stream employed.



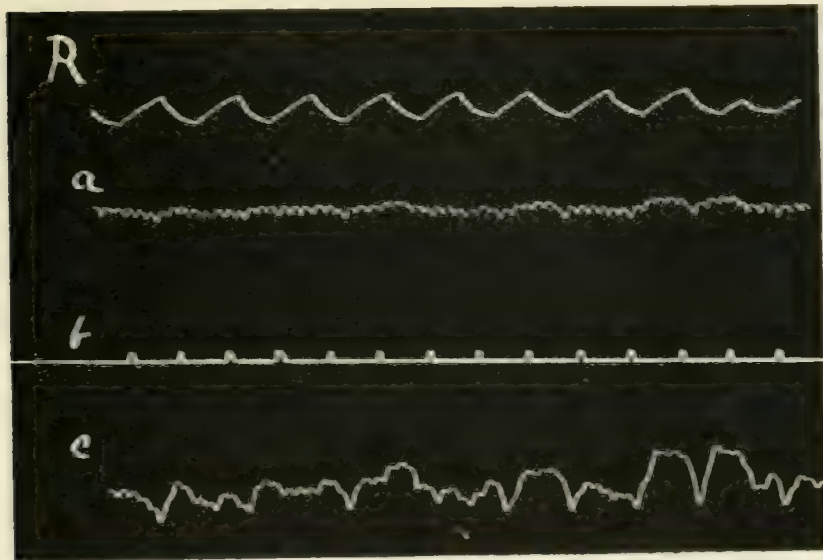


Fig. 1A.

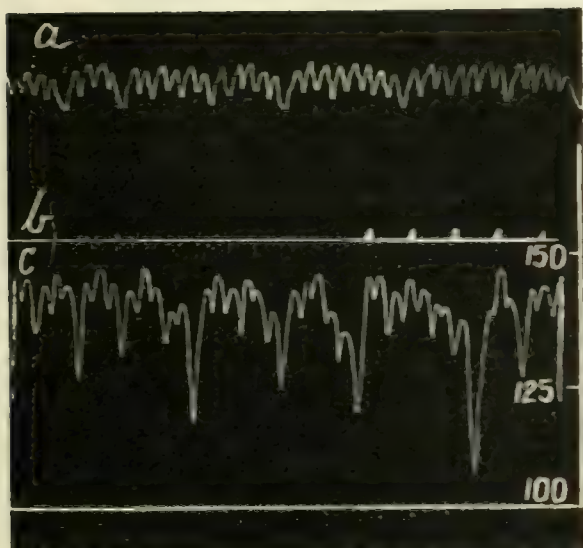


Fig. 1B.

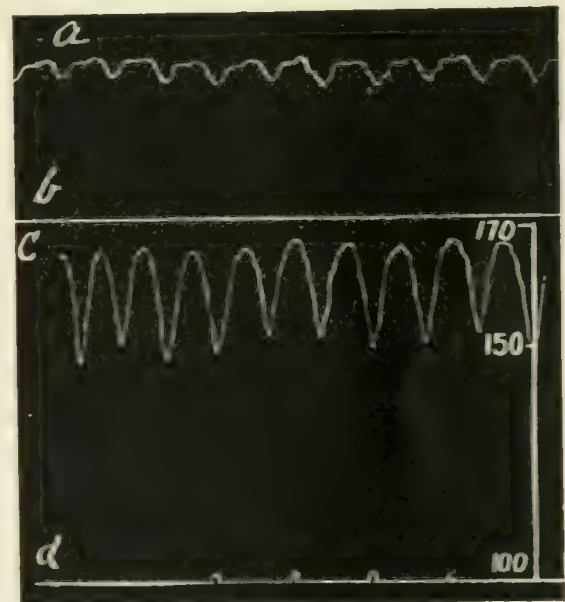


Fig. 1C.

Fig. 1. Types of irregularities occurring under light chloroform anæsthesia.

A. Hürtle and Ludwig curves recorded simultaneously from separate carotid arteries. *R*. Respiratory curve. *a*. Hürtle curve. *b*. Hürtle abscissa and time signal marking seconds. *c*. Ludwig curve. The Ludwig abscissa is not shown. These curves illustrate a rapid type of irregular tachycardia under chloroform. The Hürtle manometer accentuates the individual pulse beats, often, as in this case, with little appearance of irregularity. The mercury manometer accentuates the irregular nature of the curve, but obliterates the individual beats. The fluctuations in pressure bear no relation to the respiratory rhythm. Rate of beat—270 to 300 per minute.

B. Contrasted Hürtle and Ludwig curves, recording consecutive periods of an irregular tachycardia with beat rate of 180 per minute. *a*. Hürtle curve. *b*. Hürtle abscissa and time signal marking seconds. *c*. Ludwig curve. *d*. 100 mm. mercury pressure level.

C. Contrasted Hürtle and Ludwig curves, recorded during consecutive periods of a simple form of irregularity, *i.e.*, bigeminal beats. *a*. Hürtle curve. *b*. Hürtle abscissa. *c*. Ludwig curve. *d*. 100 mm. mercury pressure level, and time signal in seconds.

The Ludwig curves appear to represent a regular and slow beat of 90 per second. The Hürtle curve demonstrates the beats as bigeminal and the rate doubled (180 per second).

results especially are valueless under such conditions, frequently the best results are only obtained in animals in which the necessary dissections had been previously carried out and much of my work was performed upon such surviving animals.

Artificial respiration was employed for exceptional experiments only, and such exceptions are stated in the text. Ventricular irregularities are less readily exhibited in animals under its influence.

### *Definitions.*

(1) The terms *light* and *deep anæsthesia* require definition. They can be expressed largely in terms of the percentage administered, but not precisely, for the degree of anæsthesia is likewise affected by the *duration* of the administration—thus an animal may be only lightly anæsthetised by a short duration of a high percentage, a fact which has in the past led to confused inferences; the converse is also naturally the case. With these reservations a vapour of 1% or thereabouts may be taken to imply light anæsthesia, but the lighter the anæsthesia the more favourable are the conditions for the production of ventricular fibrillation, and this applies not only to the experiments with adrenalin but in the case of most of the remaining methods employed to bring it about. It is important to note that the fact of the animals being lightly anæsthetised does not imply an anæsthesia insufficient for ordinary light operations, in fact it has frequently been my practice to work with animals entirely unrestrained either in head or limb, the only fixed connection being the arterial cannula clamp. Powerful sensory stimulations such as the excitation of a sensory nerve with a strong faradic current under such circumstances naturally sometimes produce reflex movement, but all ordinary manipulations were performed without difficulty and without interference with the recording apparatus although the anæsthesia came within my category of light anæsthesia.

(2) The symbol "V.F." is employed to represent the words "ventricular fibrillation" in the tabulated accounts of experiments.

(3) The term "multiple tachycardia" is employed to denote a rapid sequence of ventricular extrasystoles arising from multiple foci.

### *Types of irregularities.*

Several well defined types of irregularities occurring under chloroform have been previously fully described and illustrated.<sup>21</sup> In addition to these it is common to observe disorderly successions of normal and irregular beats presenting various complicated records which cannot be analysed by manometric methods alone. Such types of irregularities are exemplified in Fig. 1, and many of the succeeding figures.

### *Recovery from ventricular fibrillation.*

Ventricular fibrillation is recognised as the most deadly form of cardiac syncope, in fact it was at one time a moot physiological point whether the heart ever recovered from it. As the result of an extensive experience of this



condition I am able to state that spontaneous recovery in the cat is not infrequent; it may occur after a few seconds of fibrillation (Fig. 2 and 10) or indeed after a period of one or more minutes (Fig. 11). As a general rule, however, the heart neither recovers spontaneously nor can it be restored to its normal functions by any method in general use for the treatment of cardiac syncope, and it eventually dies from asphyxia of its tissues. It does appear, however, that the proportion of recoveries may be increased by certain special measures, direct rhythmic compression of the ventricles being particularly effective, but the discussion of these matters I reserve for a later communication.

## I. THE DIRECT CARDIAC EFFECT OF ADRENALIN.

### (a) *Aspects of the reaction of general application.*

The adrenalin reaction has been so fully dealt with elsewhere<sup>14 18 & 21</sup> that a very brief re-statement will suffice for the purposes of this paper. In animals anæsthetised with chloroform to a full surgical degree the reaction consists of the usual rise of blood-pressure with or without the accompaniment of a ventricular tachycardia, never followed by ventricular fibrillation. Under light chloroform anæsthesia the tachycardia is invariable, and in the great majority of instances permanent ventricular fibrillation ensues.

These observations have now been very fully established by a large number of experiments with this drug; they are of fundamental importance in relation to the study of ventricular fibrillation under chloroform. The reaction is modified by various conditions which it is unnecessary to deal with fully in the present paper, but given a healthy animal with a well-sustained circulation and inhaling chloroform at a low percentage, the respiration being natural and unembarrassed, then the intravenous injection of 0.065 m.g. of adrenalin chloride, or frequently of a less amount, entails the almost certain onset of ventricular fibrillation.

Ventricular fibrillation produced in this, or indeed in any other way under chloroform, is generally permanent, and the heart dies from cessation of the circulation. Occasionally the heart recovers spontaneously, it may be in a few seconds or again after a period of minutes, sometimes only to fail again (Fig. 2), sometimes to resume its functions permanently. The tendency to recovery is more pronounced the smaller the dose of adrenalin, and, a point of great practical importance, the deeper the degree of anæsthesia. In the case of an injection being performed under artificial respiration the tendency to recovery is likewise increased.

The cessation of the heart's action from ventricular fibrillation occurring under the influence of chloroform is abrupt and complete. The sudden fall in the blood-pressure, which constitutes such a striking feature in many of the tracings reproduced, occurs in fact absolutely simultaneously with the onset of fibrillation. This was seen to be the case in simultaneous manometric and galvanometric curves in which corresponding points could be identified



with certainty. Moreover, the onset of a full period of fibrillation is unmistakably and immediately evident to the naked eye when the heart is at the time exposed, and is readily enough differentiated visually from the complicated irregular action of the heart which precedes it. This fact was demonstrated by depressing a signal key on observing the onset of fibrillation in an exposed heart, the signal marks on the kymographic record being always found to correspond with the dips in the pressure curve; such a kymographic record is shown in Fig. 2.

It is made certain in this way that momentary periods of ventricular fibrillation may occur, resulting in a sudden but slight fall of pressure only, for rapid recovery of the heart precludes a very low fall. Such short periods certainly may not be always easy to differentiate with the eye from the intermixed periods of multiple extrasystoles, although they are perfectly indicated on the manometer tracing, and I think that such an intermingled sequence of short but definite periods of fibrillation and tachycardias may possibly in some cases create an impression of transitional conditions: I am referring simply to my own special experiences, and I do not wish to infer that modified forms of fibrillation may not occur under some other conditions. For all practical purposes therefore I regard the cessation of the heart's action and the consequent fall of blood-pressure as a definite means of discriminating between fibrillating and non-fibrillating ventricles, and I do not, at least in respect of these chloroform experiments, regard the ventricles as truly fibrillating in any case in which the blood-pressure is sustained.

The occurrence of ventricular fibrillation may be confirmed by cutting open the chest and slitting up the pericardium as rapidly as possible after the fall of blood-pressure. The ventricles may then be found in the first or coarse stage of fibrillation, but if inspection be longer delayed the second stage may be encountered; the ventricles are then found in a state of relaxation and exhibiting faint fibrillary twitchings, which may be only perceptible on close inspection of the region of the intraventricular septum. A test may be performed for the presence of true fibrillation, when otherwise doubtful, by firm rhythmic compression of the heart, for this tends to restore the initial, and more readily visible, stage of fibrillation. The auricles, if inspected at a sufficiently early stage, may be found actively fibrillating, but this condition soon passes off, and a feeble rhythmic beat supervenes which may continue for a very long time. If, as is usually the case, the animal dies under conditions of full vascular aeration, then the left auricle is bright red and the right purple in colour.

A precipitate fall of blood-pressure from a high or moderate pressure level under chloroform and in sequence to a stage of irregular tachycardia may be taken as invariably indicative of ventricular fibrillation. At first I systematically inspected the heart after syncope, whether induced by adrenalin or by any other means, and I *invariably* found the ventricles exhibiting fibrillary contractions. Latterly therefore I have not in every case confirmed the reaction in this way, as it is unnecessary, the sequence of



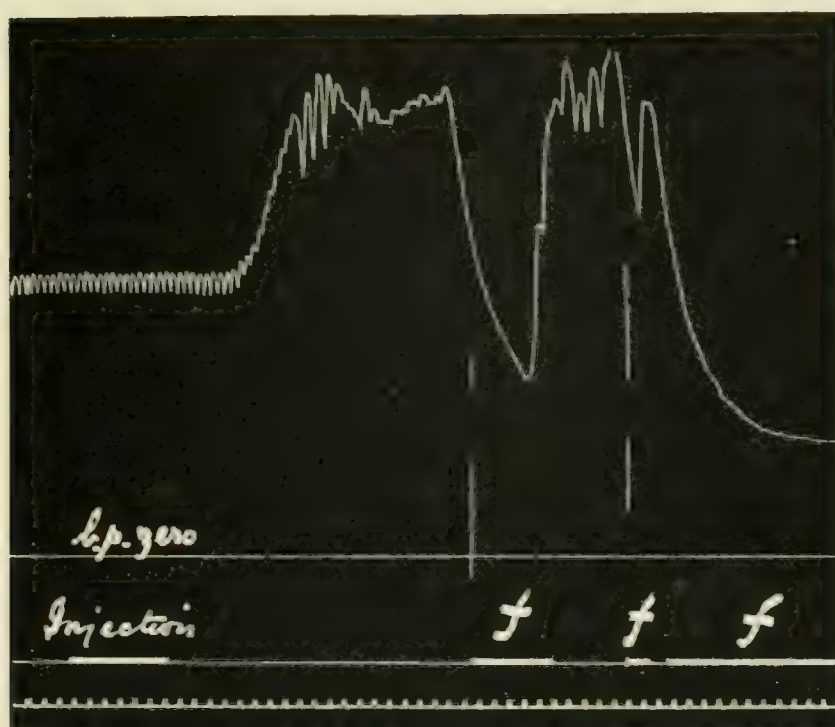


Fig. 2.  $\times \frac{3}{4}$ . Ludwig manometer curve showing how periods of V.F. may be observed in the exposed heart and correspond to dips in the recorded blood-pressure curve. The signal marks f, f, f, were made by depressing the signal key when the ventricles were observed to pass into a condition of fibrillar contractions. These periods were definitely differentiated by inspection alone from the condition of multiple extrasystoles which preceded and succeeded them, and the signal marks are seen to synchronize with the deep dips in the blood-pressure curve. The chest wall and pericardium were laid open and artificial respiration maintained with 0.5% chloroform. Adrenalin 0.2 mgms. injected into the saphenous vein. Time in seconds.

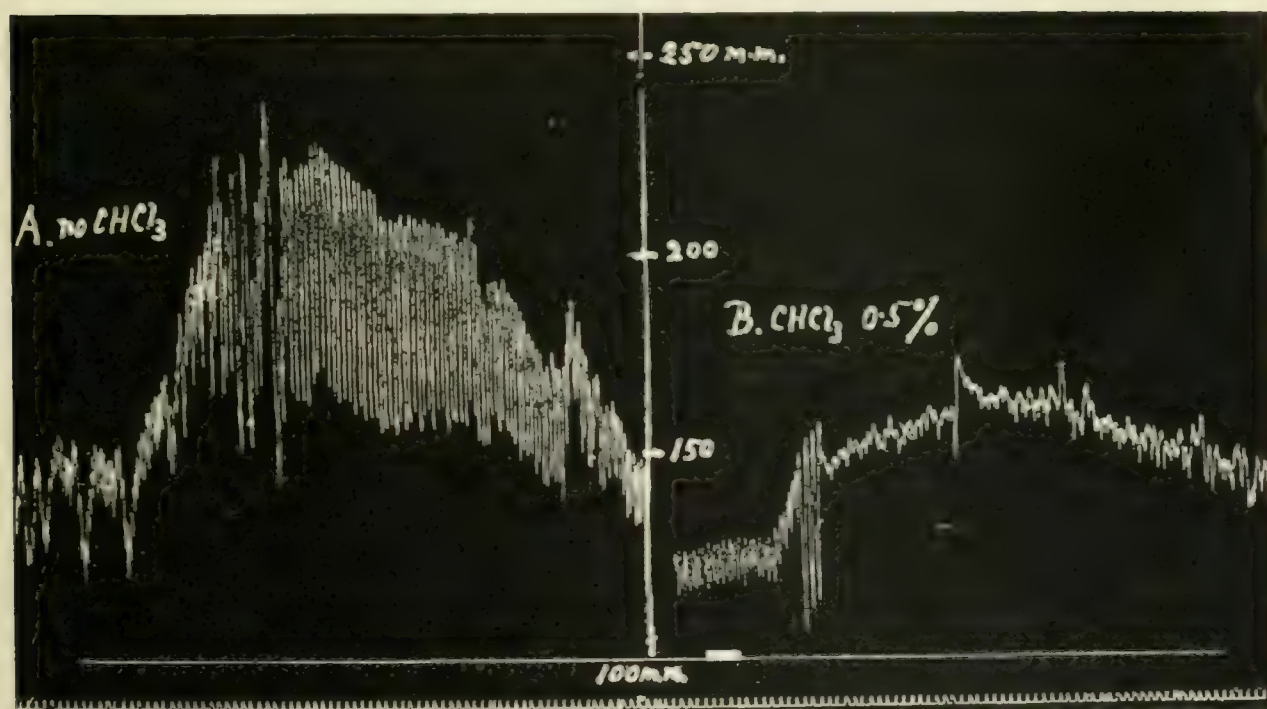


Fig. 3.  $\times \frac{3}{4}$ . Contrasted consecutive Ludwig curves from the same animal, showing the result of an intravenous injection of 0.065 mgms. of adrenalin, A. when not under chloroform, B. when under 0.5% chloroform. In A. the heart beat is slowed and regular, the initial intermissions being due to volitional movements. In B. the heart passes into a condition of multiple tachycardia. Cannula in crural artery. The abscissa line has been raised to the 100 mm. pressure level, and the vertical index represents higher pressures. Time in seconds.

events being absolutely diagnostic. I may add that I have never observed a sudden cardiac syncope in sequence to a regular heart beat in any of the experiments described in this paper.

A series of asphyxial gasps follow sudden cardiac syncope, and form a notable feature in death from ventricular fibrillation under chloroform. They demonstrate that the respiratory centre is active and not depressed by the action of the anæsthetic, and are more or less marked according as anæsthesia is deeper or lighter at the moment, and in the lighter degrees they are accompanied by a state of asphyxial spasm of the whole body; desultory respiratory efforts may continue long after the failure of the heart. A tracing of this respiratory phenomenon as a result of adrenalin injection has elsewhere<sup>14</sup> been shown, and another example (Fig. 19) is given in the course of this paper to illustrate that a precisely similar result occurs as a consequence of ventricular fibrillation produced by other means. On recovery of the heart from fibrillation the respiration again recovers itself, and on recurrence of fibrillation the exaggerated phase is again repeated, and thus it may happen that the actual process at work may be somewhat obscured in the case of a death from ventricular fibrillation, in the absence of a graphic record of events.

(b) *Control experiments.*

These were performed by injecting adrenalin into animals not under the influence of any anæsthetic, and subsequently repeating the injection after the administration of chloroform.

Two methods were employed:—

(i). Limited to a single experiment. The curves were taken from an intact animal by the method of Brooks,<sup>2</sup> and are shown in Fig. 3. The first curve, resulting from the injection of adrenalin\* when the animal was not under the influence of any anæsthetic, is characterised by a retardation of the heart beat, which remains regular. There are intermissions in the first part of this curve, but I doubt if these are really due to single extrasystoles; they are sufficiently explained by the animal happening to move at this moment—for the duration of the rest of the curve it remained perfectly quiescent. The second curve was taken after chloroform anæsthesia had been induced, the percentage being reduced to 0.5% at the time of the injection; it is fairly typical of a chloroform tachycardia as registered by a mercury manometer, but this experiment proved to be an exceptional case, for the tachycardia did not terminate in fibrillation. The dose of adrenalin in each instance was 0.065 mgms.

(ii). The animal was rendered anæsthetic in the first place by pithing the cerebrum and subsequently put under chloroform. Five experiments of this kind were performed. Under such circumstances adrenalin causes a large rise of blood-pressure in the absence of chloroform, but even when employing

---

\* The injection was made under cocaine into the crural vein, which had been previously exposed in preparing the crural artery.



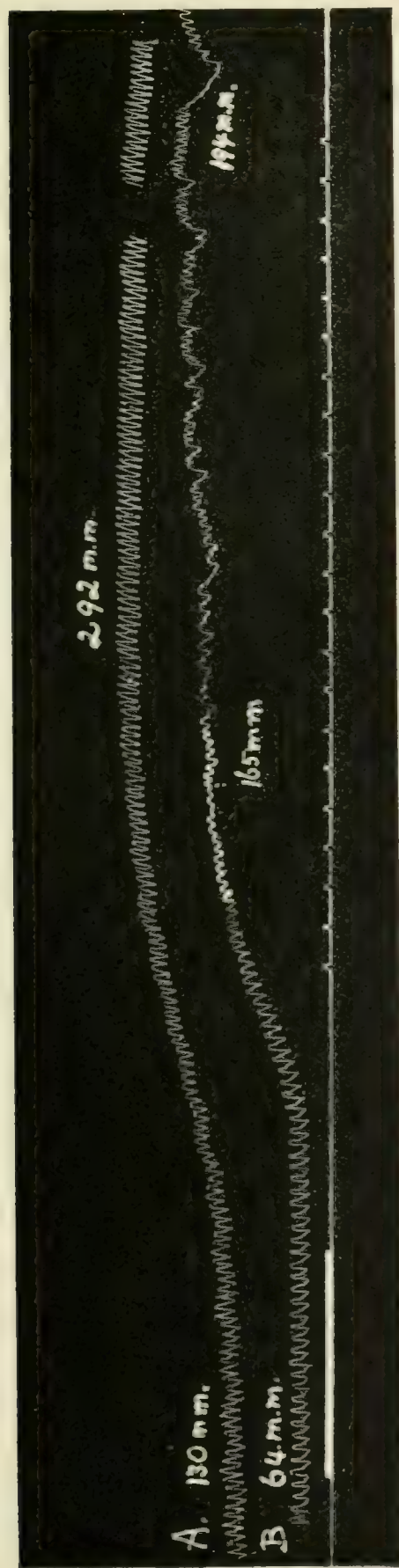


Fig. 4.  $\times 3$ . Contrasted Hürtle curves taken in sequence from the same animal; A. rendered anaesthetic by pithing the cerebral hemispheres and not under the influence of chloroform; B. under 0.5% chloroform. The curves have been superimposed for convenience of contrast, the signal line being adjusted to serve as abscissa line to both curves. The vagi had been previously cut and large doses (0.2 mgms.) of adrenalin were injected. The signal mark serves to indicate the moment of injection in both cases.

In A., the heart beat is accelerated but remains regular. In B., the heart passes into an irregular tachycardia with a well marked period of fibrillation toward the end of tracing.

The numbers inscribed indicate mean blood pressure values registered by means of a damped Ludwig manometer (not shown). Artificial respiration. Time in seconds.

abnormally large doses, I have not observed any trace of irregularities. The pulse rate under such conditions may be affected in either direction (out of five experiments acceleration occurred in three and retardation in two), but otherwise the beat is unaffected and the tracing is generally remarkable for its perfect regularity. When, however, chloroform is administered to an animal treated in this fashion, then, although adrenalin does not invoke a permanent fibrillation of the ventricles,\* yet the usual sequence of intense irregularities, often with momentary periods of fibrillation, is brought about. Paired observations of this nature are illustrated in Fig. 4 and 5. In the experiment from which Fig. 4 was taken the vagi had been cut and large doses (0.2 mgms.) injected in order to obtain a full effect; in the curve taken without chloroform the beat was rapid both before and after the injection, but slightly accelerated after; the beats were powerful and normal beats, as was confirmed by reference to the simultaneous damped mercury manometer curve (not shown in the figure) in which every beat was well defined, with well-marked respiratory curves and without a trace of the irregular dips in pressure which are so characteristic of extrasystolic tachycardias. In Fig. 5 are shown a contrasted pair of curves registered by the undamped mercury manometer, the vagi being uncut and the usual small doses of adrenalin being administered.

The foregoing experiments clearly demonstrate that adrenalin has not any innate power of producing ventricular irregularities, but that it acts as an *exciting cause only* when the heart is rendered sensitive by chloroform. This statement is at variance with the observations of Kahn,<sup>11</sup> which have been generally regarded as indicating that multiple tachycardias are a frequent and normal sequence of adrenalin injections (*cf.* electrocardiogram No. 16 in his paper), but Kahn's experiments are vitiated by reason of his experiments being performed with animals deeply under a general anæsthetic, a mixture containing chloroform (chloroform 9, ether 30, petroleum ether 3), and this fact brings his observations into conformity with my own.

### (c) *The cardiac action of adrenalin.*

The action of adrenalin on the heart is a local one and not induced through central nervous agency. This was proved by isolating the heart from all nervous connections. The isolation was performed very thoroughly by extirpating the stellate ganglia or by section of their cardiac branches, together with section of the vago-sympathetic trunks in the neck; the spinal cord was destroyed in addition in some instances, in one case the bulb also. Six experiments were performed and in five of them the heart fibrillated. The following experiment will serve as an example.

---

\* This has since been attributed to a stimulation of the vagal centres by the act of pithing and by the subsequent high intracranial pressure.



*Experiment, August the 15th, 1912.* Both stellate ganglia excised at a previous operation. Vagi cut. Spinal cord destroyed by passing a stylet down the vertebral canal under artificial respiration.

The injection of 0.065 mgms. of adrenalin chloride into a saphenous vein under 0.5 per cent. chloroform induced V. F. in 22 seconds.

In Fig. 6 is shown a tracing of a similar experiment. The curve is somewhat unusual in connection with adrenalin in showing an early period of what are, apparently, slowed beats, but which close inspection of the original curve shows to be conditioned by a bigeminy due to extrasystoles.

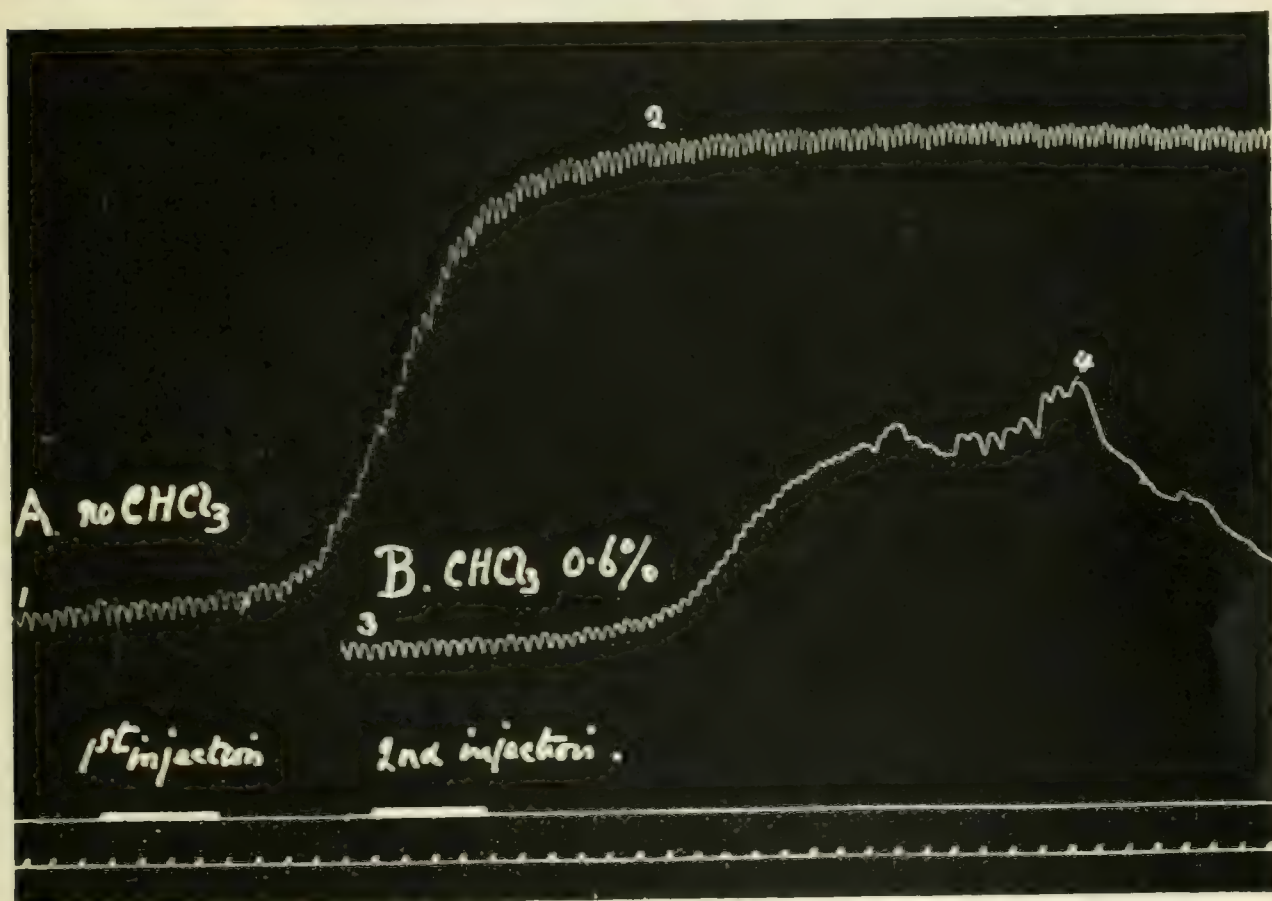


Fig. 5.  $\times \frac{3}{4}$ . An experiment performed under similar conditions to that described in the preceding figure. Ludwig manometer employed in this case. The vagi were not cut, and ordinary doses (0.065 mgms.) of adrenalin injected. The signal line had been adjusted to serve as the abscissa to both pressure curves. The numbers serve as a reference to blood-pressure levels as follows: (1) = 74 mm.; (2) = 200 mm.; (3) = 64 mm.; (4) = 130 mm.

(d) *The reaction in chloroformed dogs.*

The reaction in dogs is similar to that in cats, but a larger dose of adrenalin is apparently necessary, *e.g.*, 0.13 mgms. The tachycardia produced, so far as I have observed it, is not so rapid as in the case of cats.

(e) *The adrenalin reaction in the chloroformed human subject.*

A communication<sup>18</sup> in regard to this matter was recently read before the British Medical Association, and it was therein shown that fatalities have occurred from the ill-advised use of adrenalin for surgical purposes and for the treatment of shock in patients under chloroform. It was shown, moreover,

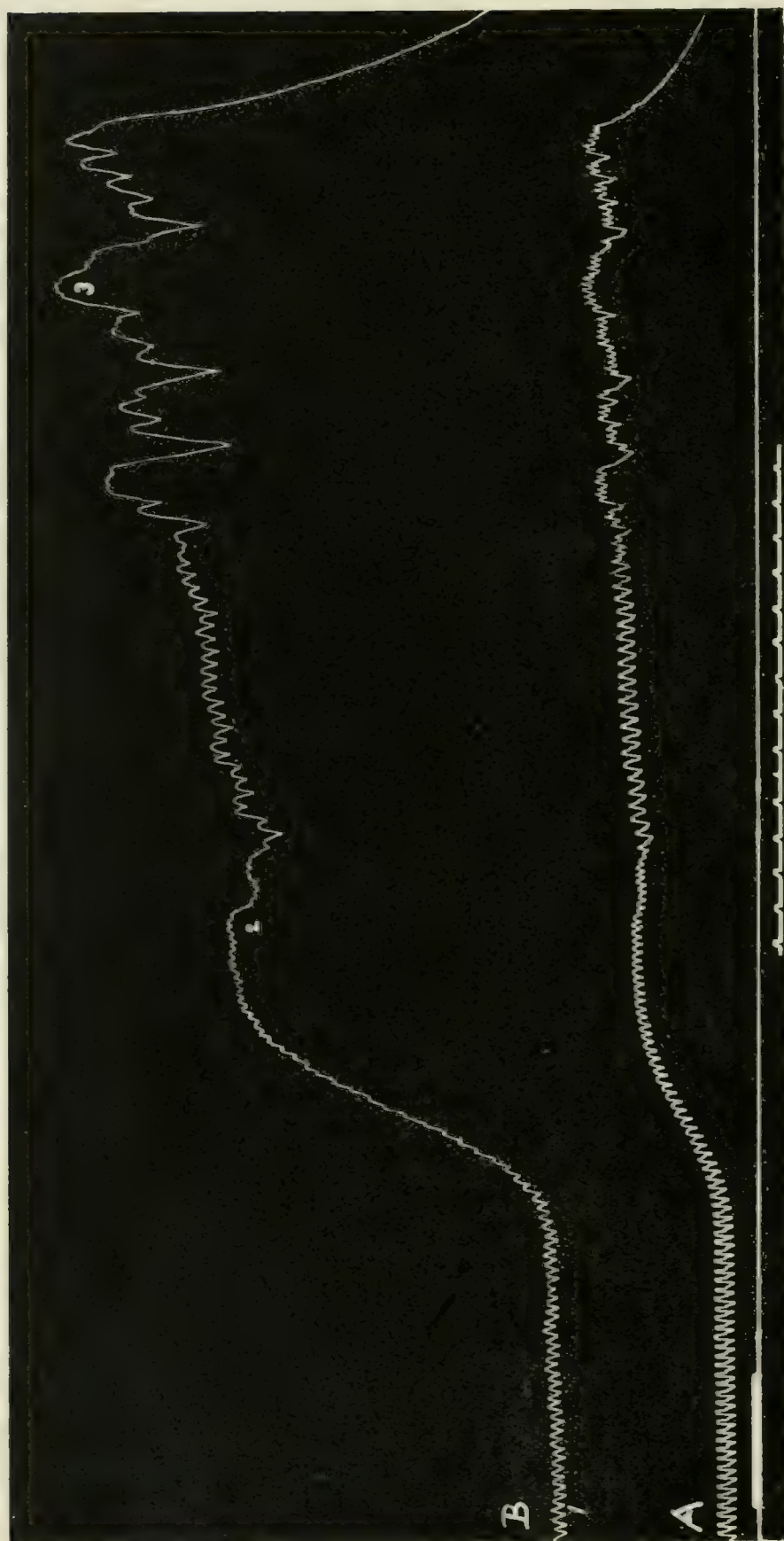


Fig. 6.  $\times \frac{2}{3}$ . Simultaneous Hürtle (A) and damped Ludwig (B) curves showing the action of a large dose (0.2 mgms.) of adrenalin in a cat under chloroform in which the heart had been isolated from central nervous influences. The vago-sympathetic nerve trunks were cut in neck, the cardiac branches of both stellate ganglia were cut and the spinal cord was destroyed by passing a stylet down the vertebral canal. Artificial respiration with 0.5% chloroform. The signal mark represents the moment of injection. The signal line has been adjusted to serve as abscissa line to both curves. The heart is regular before injection. A rise of blood-pressure with cardiac acceleration is the first effect of the injection. The blood-pressure falls with the first onset of cardiac irregularity (2). The heart then passes into a phase of slowed action, the slowing being seen on careful inspection to be due to periodic extrasystoles. The next phase is one of a very irregular tachycardia of about 360 beats per minute, and finally the blood-pressure rapidly falls to zero as a result of ventricular fibrillation. The numbers denote blood-pressure levels as follows: (1) = 69 mm.; (2) = 174 mm.; (3) = 232 mm. Time marked in seconds.



that the anæsthesia was a light one at the time of the injection and that the mode of death was similar to that which occurs in cats under similar conditions.\* The only difference noted was a pronounced tendency to recovery in the human subject.

A further fatality of this kind has been reported just recently (*Brit. med. Journ.*, 1913, I, 879). The following is a brief abstract :—

“The patient was a male aged 26, a well-developed and healthy man. Operation for deflected nasal septum.”

“Anæsthesia was induced by chloroform given upon a Skinner’s mask, and it was decided to inject some adrenalin into the nose subcutaneously. At the time of the injection anæsthesia was light (a brisk corneal reflex being obtainable), the pulse strong, and the patient’s colour good. No more chloroform was given.”

“About one minute after the injection the pulse suddenly became very rapid and then imperceptible; at the same time the patient’s colour became leaden grey and the pupils widely dilated. About three deep gasps were taken after the pulse had failed, and then respiration ceased.”

## II. THE DIRECT CARDIAC EFFECT OF EXCITATION OF THE ACCELERATOR NERVES.

If we dismiss the general pressor action of adrenalin from consideration and regard ventricular fibrillation as resulting from the excitory influence which adrenalin exerts upon the myoneural junction of the sympathetic nerve supply of the heart, then it is evident that confirmation of this view should be obtained by exciting these same junctions through ordinary physiological channels, *i.e.*, through the accelerator nerves themselves. Such an experimental procedure does in fact confirm this view of the action of adrenalin in a convincing and complete manner. A short note<sup>16</sup> has already appeared touching on this subject, but it requires some further reference here.

The experimental procedure adopted was as follows: The cat was anæsthetised in the usual way, care being taken to avoid any unnecessary excess of chloroform throughout. The right stellate ganglion was exposed by Anderson’s dorsal operation between the heads of the first and second ribs and all its connections were divided with the exception of the two post-ganglionic cardiac nerves. A carotid artery was then prepared and connected with the manometer. The ganglion was caught up on electrodes hooked in between the cardiac branches, and was stimulated with a faradic current. The result of this stimulation upon the heart in the presence of a weak percentage of chloroform is almost precisely the same as that resulting from the injection of adrenalin, *i.e.*, the ventricles pass from a condition of regular rhythmic contraction into one of multiple arrhythmic tachycardia terminating in ventricular fibrillation (Fig. 7 B). The onset of irregularities and of fibrillation may be very rapid, the latter may in fact occur within seven seconds from the commencement of the stimulation, but it is more frequently delayed for some 30 seconds.

TABLE I.

| No. | Preparation of                    | Chloroform percentage | Excitation Coil at | Left Ganglion excited | Right Ganglion excited.     |
|-----|-----------------------------------|-----------------------|--------------------|-----------------------|-----------------------------|
| 1.  | Right ganglion                    | 0.5                   | 55 mm.*            |                       | V.F.                        |
| 2.  | Right ganglion.                   | 0.5                   | 100 mm.            |                       | V.F.                        |
| 3.  | Right ganglion and both vagi cut. | 1.8                   | 93 mm.             |                       | V.F. of 3 seconds duration. |
| 4.  | Right ganglion.                   | 0.5                   | 93 mm.             |                       | V.F.                        |
| 5.  | Right ganglion                    | 0.5                   | 100 mm.            |                       | V.F.                        |
| 6.  | Right ganglion.                   | 0.5                   | 93 mm.             |                       | Irregularities only.        |
| 7.  | Right ganglion.                   | 0.5                   | 93 mm.             |                       | V.F. of 2 seconds duration  |
| 8.  | Right ganglion.                   | 0.5                   | 93 mm.             |                       | V.F.                        |
| 9.  | Right ganglion.                   | 1.0                   | 70 mm.             |                       | V.F.                        |
| 10. | Right ganglion.                   | 0.5                   | 100 mm.            |                       | Irregularities only.        |
| 11. | Right and left ganglia.           | 0.5                   | 93 mm.             | Slow tachycardia      | Rapid tachycardia.          |
| 12. | Right and left ganglia.           | 1.5                   | 55 mm.             | No irregularity.      | V.F.                        |
| 13. | Left ganglion.                    | 0.5                   | 55 mm.             | Slow irregularities.  |                             |
| 14. | Left ganglion.                    | 0.5                   | 100 mm.            | V.F.                  |                             |
| 15. | Left ganglion                     | 0.5                   | 75 mm.             | Slight irregularity.  |                             |

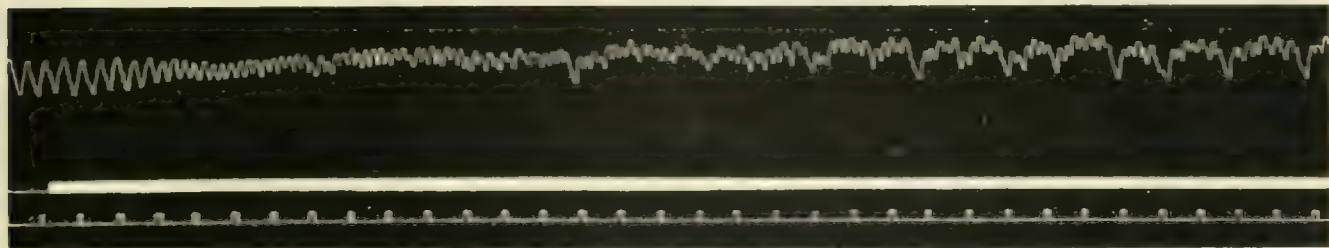
\* With the coil at 95 mm. the current was just too painful to be applied to the tongue.

The above table provides an abstract of the whole of my experiments upon excitation of the stellate ganglia, not precisely in the order of their performance, but grouped for purposes of tabulation. In many of them a number of excitations at higher percentages of vapour preceded those tabulated, but these were ineffectual in producing ventricular fibrillation.

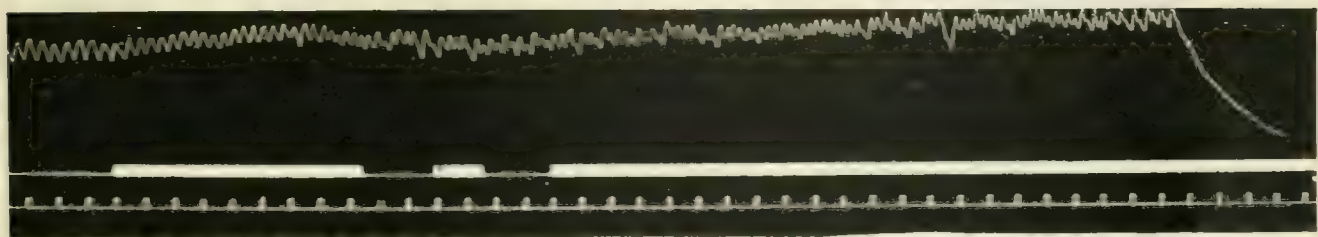
The outstanding feature of this series of experiments is the frequent incidence of ventricular fibrillation from excitation of the right ganglion under low percentages of vapour. In Experiment No. 12 the percentage



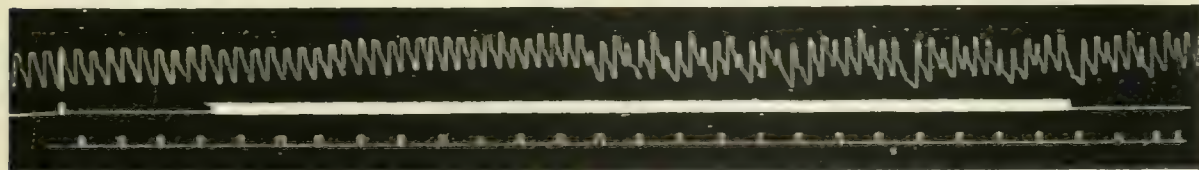
indicated was 1.5%, but the animal was only moderately anæsthetised. In Experiment No. 3 fibrillation was obtained at 1.8%, the animal being apparently well under the anæsthetic, but in this case the vagi had been previously severed, a factor which must be taken into account. This heart recovered in three seconds. In all other instances on stimulation of the right ganglion at 2% or thereabouts, the heart either remained regular, or, as was more frequently the case, assumed a condition of a rapid irregular tachycardia, with possibly a mere flicker of fibrillation, but never coming to a complete standstill (Fig. 7 A).



(A)



(B)



(C)

Fig. 7. Excitation of a stellate ganglion under chloroform, all nervous connections of the ganglion, with the exception of the cardiac branches, having been cut. The tracings were not taken from the same individual. Hürtle manometer. The signal line serves as abscissa in each case. The excitation was faradic, with the coil at 95 mm. Time marked in seconds.

A. Right ganglion excited under 2% chloroform. A multiple tachycardia is induced but the ventricles do not fibrillate.

B. Right ganglion excited under 0.5% chloroform. A similar tachycardia is produced but terminating in ventricular fibrillation in 37 seconds.

The gaps in the signal mark are due to temporary failure of the interrupter.

C. Left ganglion excited under 0.5% chloroform. A tachycardia is induced, but it is of a less intense type than that seen on excitation of the right ganglion.

The result of stimulation of the left ganglion is dissimilar—rapid irregularities are seldom seen from this side, and the curve shown in Fig. 7 C is typical of the result which is generally obtained.\* In experiment No. 14 alone was fibrillation produced, the heart in this case being very irregular before the excitation was made.

\* Possibly this difference is subject to a purely anatomical explanation, for the left stellate ganglion is smaller than that on the right side in the cat.

Experiment No. 3 may be specially cited as showing that the stimulation of the heart through the accelerator nerves exercises its effect upon the chloroformed heart through its own influence alone and independently of any relation to a concurrent vagus tonus ; in fact the previous removal of vagal influence appears to favour the onset of ventricular fibrillation at a higher grade of chloroform anæsthesia than is usual. The details of this experiment are as follows :—

TABLE II.

| CHLOROFORM. |  | PULSE RATE. | REMARKS.  |
|-------------|--|-------------|---|
| 2%          |  | 84          | Beat regular.   |
| 2%          | Vagi cut.                                      | 180         | Beat regular.   |
| 1.8%        | Stimulation to right stellate, coil at 100 mm. | 320         | Tachycardia culminating in V.F. of 3 seconds' duration. |

Many workers have sought to obtain ventricular fibrillation through accelerator action. Of these the most successful, hitherto, have been Rothberger and Winterberg,<sup>25</sup> who obtained abnormal beats, in dogs subjected to the narcotic influence of morphia and curari, by combined vagal and accelerator stimulations, and in rare instances they obtained ventricular fibrillation. In a further series of experiments on dogs under ether, and further submitted to the influence of moderate doses of barium chloride, they invariably obtained complex ventricular tachycardias on stimulating the left accelerators, but they do not appear to have attained any greater measure of success in respect of producing ventricular fibrillation in this series than they did in their former series.

The action of chloroform, described above, of rendering the heart irritable and causing it to react in an abnormal fashion to accelerator influences is thus far unique in respect of its potency.

### III. CARDIAC EFFECTS ARISING AS A REFLEX FROM SENSORY STIMULATION.

Bearing in mind the foregoing demonstration of ventricular tachycardias and fibrillation excited through the agency of the accelerator nerves, it might be anticipated that similar effects would be induced through reflex mechanisms by the excitation of sensory nerves ; as a matter of fact, every cardiac effect previously described may be reproduced in such a manner. The heart responds very readily to sensory stimuli by passing into an irregular condition just as it does under the influence of adrenalin or of accelerator excitation ; and in just the same way the reaction is modified by the depth of the anæsthesia. At 2% or over the onset of irregularities is uncertain, and if they do appear they may exhibit various degrees of intensity, but they never pass into ventricular fibrillation. Under lighter degrees of anæsthesia, 1%



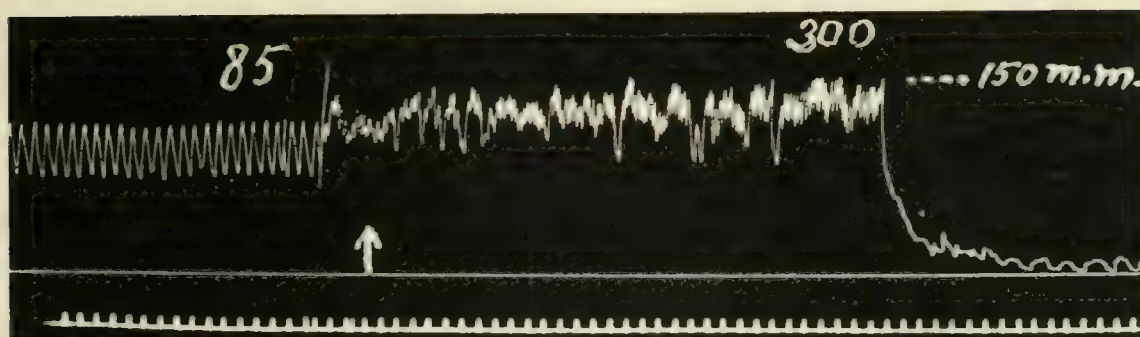


Fig. 8. Hürtle curve showing tachycardia and subsequent V.F. induced by cutting a sciatic nerve. The first part of the tracing shows a regular slow beat (bigeminal?) occurring under a moderate degree of anæsthesia, percentage not measured. The sciatic nerve was cut with a pair of scissors, whilst the drum was stationary, at the vertical line. The mechanical excitation caused a reflex stimulation of the heart and the consequent onset of an irregular tachycardia. The chloroform was removed at the arrow mark, and 30 seconds after this the blood-pressure fell from 150 mm. to zero as the result of ventricular fibrillation. The blood-pressure during the regular beat was 114 mm., the lowest pressure during the experiment, showing that the heart was not at any time unduly depressed by chloroform. The blood-pressure was registered as usual by simultaneous Ludwig records (not shown). The undulations seen at the end of the curve after fibrillation were caused by the terminal asphyxial gasps. The numbers above the curve represent the rate of heart beat per minute. Time marked in seconds.

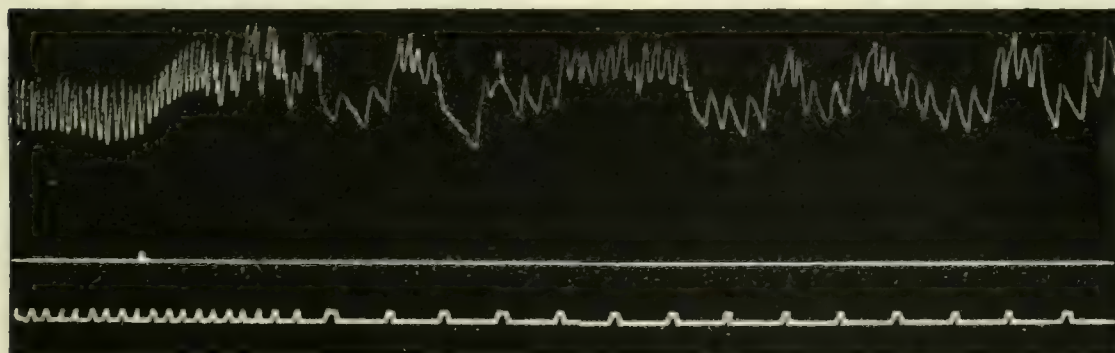


Fig. 8a. Hürtle curve showing the transition from a regular to an irregular beat arising from cutting a sciatic nerve with a pair of scissors. The signal mark indicates the moment of section. The signal line represents the Hürtle abscissa. Time in seconds. Rate of kymograph increased to analyse irregularities.

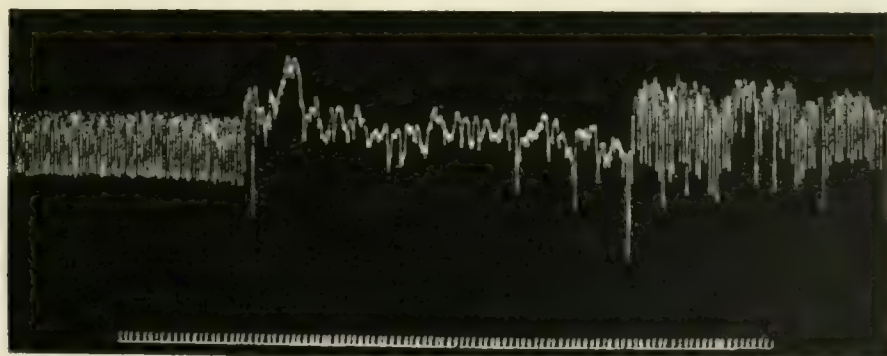


Fig. 9. Ludwig curve showing the reflex cardiac effect of applying ammonia vapour to the nostrils of a cat not long under chloroform. Strength of chloroform vapour = 1%. The time line has been raised to the 75 mm level. Time marked in seconds.

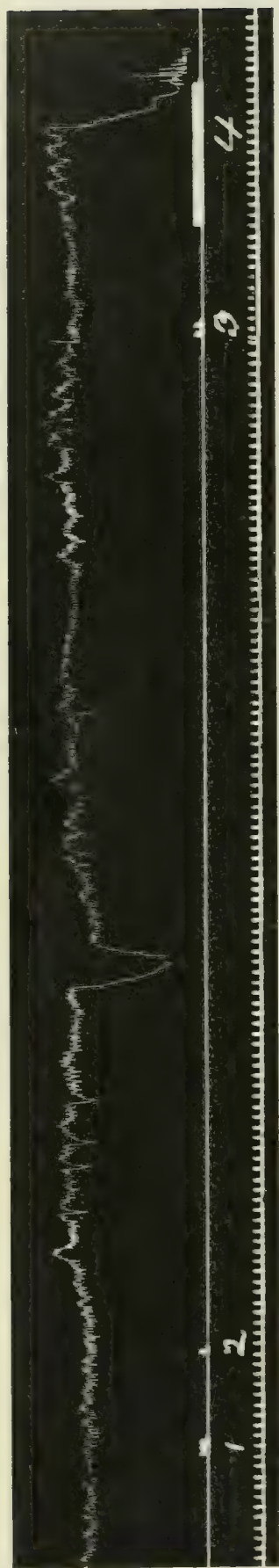


Fig. 10. Hürtle curve showing the effect of cutting the sciatic nerve (2) and stimulation of the nerve (4) in a cat under light chloroform anaesthesia. The vagi were previously cut, and the heart was exhibiting an irregular tachycardia under 1% chloroform. At (1) the chloroform had been taken off, and 0.5% vapour was given again at (3), just before the sciatic was stimulated. The mechanical excitation of section of the nerve sends the blood-pressure up from 120 to 140 mm., makes the heart more irregular, and in 32 seconds causes V.F. with recovery in 3 seconds. Faradic excitation of the nerves causes complete V.F. at a final blood-pressure of 154 mm. This cat made a complete recovery about 60 seconds after fibrillation.

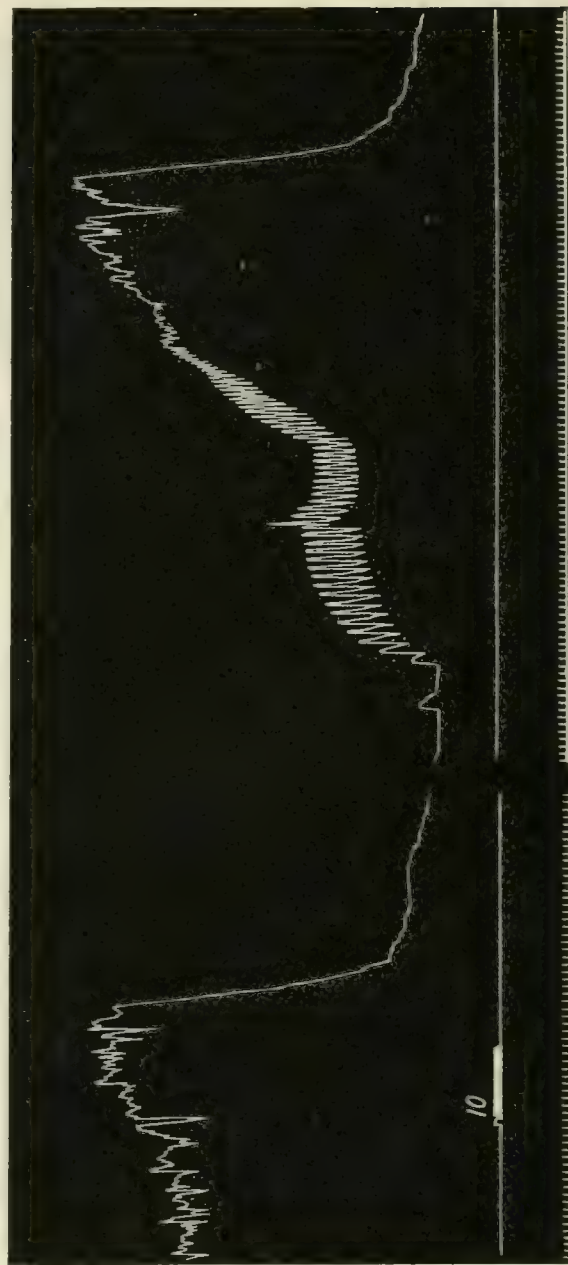


Fig. 11.  $\times 3$ . (Redrawn). Ludwig curve shows V.F. resulting from excitation of a median nerve by a faradic current with coil at 100 mm. Chloroform 0.5%. The heart recovers after about 60 seconds with a slow and regular beat, relapsing into a tachycardia and later into V.F. A second recovery and final collapse occurred in a precisely similar fashion (not shown in the figure). Artificial respiration. The signal line has been adjusted to the pressure zero. Time marked in seconds.



or under, the irregularities occur with great constancy and may present forms of the most intense description. The modifying influence of the depth of anæsthesia is illustrated in Fig. 15 in curves *a* and *b*. (Although the preparation of this animal was unusual, the curves may be taken as fairly representative.)

The irregularities thus produced may, and generally do, disappear sooner or later on the cessation of the stimulation, or being once started they may persist almost indefinitely and even sometimes be intractable to control through increasing the percentage of chloroform; or they may culminate in ventricular fibrillation if the anæsthesia be sufficiently light.

Fig. 8 and 10 illustrate the onset of ventricular fibrillation resulting from the mechanical stimulus of cutting the sciatic nerve with a pair of scissors, and Fig. 8a shows the transition from a regular beat to an irregular tachycardia from the same exciting cause.

The form of excitation adopted in most cases was that of faradic stimulation as lending itself to purposes of exact comparison, but in a fresh nerve mechanical excitation such as that of cutting or crushing, or even merely cleaning the nerve trunk, is even more active in the production of irregularities. It is not even necessary to resort to such severe measures, for excitation of sensory nerve endings such as may result from cutting the skin, or from applying an irritant, such as ammonia, to the nostrils, will often produce a similar result (Fig. 9).

It is evident, for these reasons, that all the preliminary preparations for an experiment such as exposure of the artery for connection with the manometer must be performed under a well-established chloroform anæsthesia, otherwise reflex irregularities are set up, which may be very persistent, and are generally undesirable.

The onset of the irregularities is frequently somewhat delayed as compared with the reaction time in the case of direct accelerator stimulation (although by no means invariably so), and it is a further very notable fact that after several consecutive stimulations, the reflex becomes obscured or even totally abolished; even when the later stimulations are applied to another and fresh nerve this fatigue is still much more noticeable than that which sometimes follows consecutive stimulations of the stellate ganglia. These facts are no doubt the outcome of a depression of the activity of the reflex centres through the influence of the anæsthetic. Under these more involved conditions it is not surprising that the most intense form of ventricular irregularity, *i.e.*, fibrillation, does not occur with any approach to the same frequency that it does as a result of a more direct stimulation of the heart, and that in fact its occurrence is a comparatively exceptional event. Thus out of my first series of some forty animals I only obtained ventricular fibrillation in six cases, and that not always as a permanent condition. These cases were as follows:—

1. Permanent V. F. resulted from pinching the central end of a sciatic nerve after the cessation of chloroform inhalation and 27 seconds from the commencement of excitation. The animal was still fairly under the influence of the anæsthetic when the nerve was excited and evinced no muscular reflex; the heart was exhibiting irregularities previously to stimulation.



2. (Fig. 10). In this animal both vagi were divided and the heart was in a state of persistent rapid tachycardia which had been originated by the act of cleaning the sciatic nerve. The chloroform (1%) was taken off and the left sciatic nerve was cut. In 32 seconds the ventricles fibrillated for 3 seconds and then recovered. Later 0.5% was administered and the sciatic stimulated with a faradic current; complete V. F. ensued within ten seconds of the commencement of the excitation.

3. Faradic excitation of a sciatic nerve under light anæsthesia, the heart beating regularly. An irregular tachycardia was produced passing in 13 seconds into V. F. of about 1 second duration.

4. Permanent V. F. produced by a prolonged faradic excitation (about two minutes) of a sciatic nerve. The heart beat was regular just previous to excitation. Artificial respiration with 0.5% chloroform.

5. Faradic excitation to a sciatic nerve under 1% chloroform, the heart beat being previously irregular. V. F. followed in 10 seconds. Recovery ensued after 6 seconds of fibrillation.

6. (Fig. 11). Faradic stimulation to a median nerve under 0.5% chloroform. The heart was irregular as a result of previous stimulations. Complete V. F., which persisted for about 60 seconds and was followed by recovery and again a further and final relapse.

In another and later series of eight animals the sciatic nerve was in four cases stimulated both before and after cutting the vagi, in the remaining four the vagi being left intact throughout. I obtained complete ventricular fibrillation with uncut vagi in one case, and in one other case with cut vagi. In both cases the heart was irregular before stimulation and in both the chloroform was of 0.5% strength.

The operation for exposure of the splanchnic nerves in the lumbar region is somewhat more severe than that for exposure of the sciatics, yet these nerves appear to be very sensitive in some individuals, and I obtained the high proportion of two cases of permanent V.F. out of a series of five animals in which the *central* end of a cut splanchnic nerve was excited by the faradic current. In both cases the heart was exhibiting irregularities before the nerve was stimulated, the chloroform in the one case being 0.8% and in the other 1.0%, in both cases anæsthesia was particularly well established, and there was no trace of spasmodic muscular reflex.

It may be inferred from the foregoing cases that ventricular fibrillation is more liable to occur if the faradic excitation is applied at a time when the heart is already exhibiting irregularities. I think this may be more generally the case; I have seen death occur with remarkable rapidity in several instances upon simply picking up a nerve for the purpose of placing it upon the electrodes, the heart being irregular at the moment, but of these instances I do not possess tracings.

In two of the foregoing ten cases of fibrillation, both the vagi had been previously divided—this is an important observation for two reasons: (1) it totally disposes of any suggestion that these effects are in any way connected with a reflex stimulation of the vagus centre; (2) it disposes of any suggestion that the results may be connected with reflex inhibition of the vagal tonus. Whether reflex fibrillation is favoured by thus cutting out vagal influence I have not sufficient statistics from the foregoing experiments to show, but there is some reason, as will appear from subsequent experiment and considerations, to believe that it does so.\*

---

\* Garrey<sup>6</sup> is strongly impressed with the view that vagus excitation tends to oppose the onset of fibrillation as a result of faradisation of the ventricles.



*(a) The paths of action of sensory reflexes.*

Many of the foregoing experiments were originally performed with a view to investigating a presumed relationship between the onset of cardiac

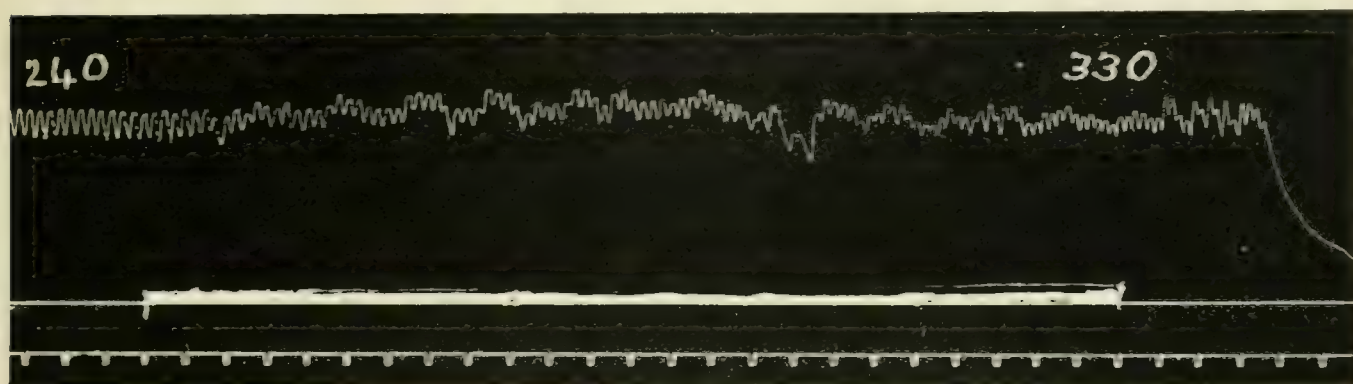


Fig. 12. Ventricular fibrillation caused by stimulation of a sciatic nerve in a cat in which both stellate ganglia had been extirpated six weeks previously. Chloroform 1%. Coil at 60 mm. The heart before excitation was regular, but rapid as a result of previous section of the vagi (rate 240 per minute). An irregular tachycardia appears within two seconds of the beginning of excitation and terminates in V.F. about four seconds after the cessation of the excitation. Blood-pressure just before V.F. = 146 mm. The numbers above the curve denote heart rate. Hürtle manometer. Time in seconds.

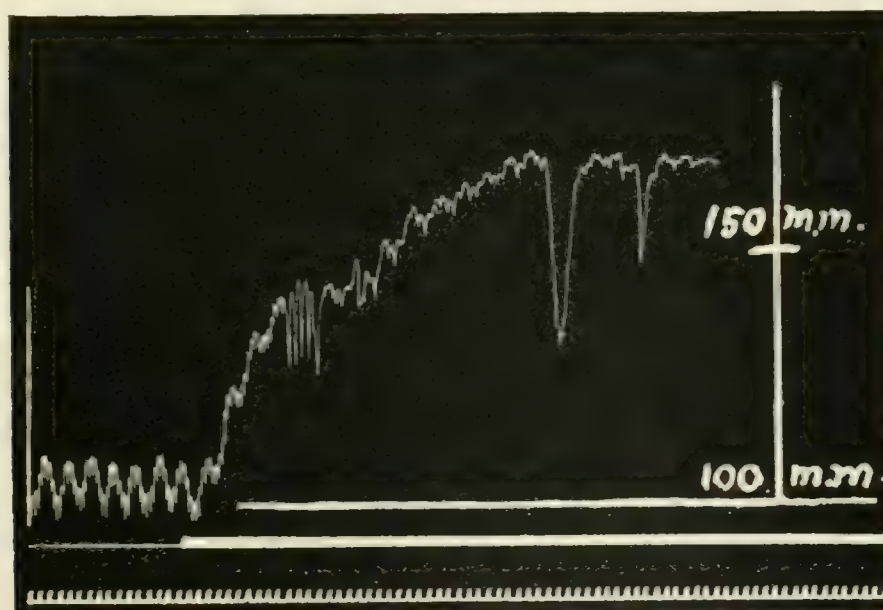


Fig. 13. Ludwig curve showing the result of stimulating the peripheral end of a cut splanchnic nerve under 1.2% chloroform. The blood-pressure rises abruptly as a result of vasoconstriction in the splanchnic area and partly as a result of secretory stimulation of the suprarenal body. In the first part of the rise the regularity of the heart beat is unaffected. The adrenalin effect commences as a series of single extrasystoles, which passes into a multiple tachycardia and temporary periods of V.F. This cat had previously received a dose of 0.13 mgms. of atropin sulphate (intravenous). The vertical scale indicates blood-pressure levels. Time marked in seconds.

irregularities and raised intra-cardiac tension dependent upon reflex vasoconstriction. The rise of blood-pressure resulting from sensory excitation is not very great under chloroform, but it is nevertheless generally quite evident. When I became aware of the action of the accelerator nerves I

sought further to test the influence of a raised intracardiac tension by severing the cardiac branches of both the stellate ganglia and thus exclude reflex accelerator action. In an experiment of this description the sciatic nerve was cut under 1% chloroform, the act of section causing the heart to pass from a regular to a bigeminal beat resulting from extrasystoles. The sciatic was then stimulated, and in 24 seconds the blood pressure having risen from 114 mm. to 134 mm., the bigeminal beat suddenly passed into an irregular tachycardia of 240 beats per minute with a fall of pressure to its earlier level.

This result was so suggestive that, in order to confirm it, I next undertook a series of experiments in which, for the purpose of excluding all possibility of accelerator action, both stellate ganglia were completely excised, the animals being allowed to survive and the final experiments performed some weeks afterwards when the cats had fully recovered from the effects of the operation.

Seven experiments of this kind were performed. In the final observations one of the hearts was exhibiting persistent irregularities from the commencement which could not be controlled and hence no satisfactory observations could be made. In one other a very few isolated extrasystoles only could be induced, but in the remaining five cats typical irregular conditions of the heart were produced by sciatic stimulation. Thus for instance :—

No. 4. Stellate ganglia extirpated three weeks previously. 1.9% chloroform. Cutting right sciatic excited a few bigeminal beats. Heart then became regular at 120 beats per minute. Sciatic stimulation, with coil at 70 mm. caused acceleration of the beat, the first extrasystole appearing 5 seconds from the commencement of stimulation; an irregular tachycardia of 270 beats per minute then appeared.

No. 7. Stellate ganglia extirpated six weeks previously. The sciatic nerve was stimulated under 1% chloroform, which occasioned the onset of reflex irregularities, and these passed into ventricular fibrillation (Fig. 12) four seconds after cessation of the stimulation. The vagi had been previously cut.

These results appeared to afford evidence that a pressor action was indeed an exciting cause of ventricular irregularities under chloroform, and such a view was in conformity with observations I had previously made that excitation of the *peripheral* end of a cut splanchnic nerve in intact animals would throw the ventricles into a tachycardial condition; in a single instance only did I observe fibrillation and that was of momentary duration only (Fig. 13); in these experiments there was no apparent source of reflex excitation of the heart through the accelerator nerves.

A complete explanation of these phenomena may be offered, however, quite apart from blood-pressure changes. The explanation is one which suggested itself as a possible cause of cardiac irregularities under chloroform when I first discovered the adrenalin reaction, but at the time I knew of nothing to support it. Since then papers have appeared by Cannon and de la Paz<sup>3</sup> on the secretion of adrenalin in strong emotional states, and by Elliott,<sup>4</sup> who has fully confirmed the fact that there exists a nervous control of the suprarenal secretion. This fact has evidently in the past given rise



to some confusion in physiological conclusions especially in relation to cardiac acceleration (*cf.* von Anrep<sup>29</sup>) and it had to be taken into consideration in relation to the matter under investigation, for the possibility had to be considered of adrenalin being secreted through a reflex nervous agency in sufficient quantity to determine abnormal ventricular contractions.

To test this matter further the following experiment was performed :—

*Experiment, 23/8/12.* Cat. Stellate ganglia excised five weeks previously.

Both splanchnic nerves exposed in the thorax under artificial respiration with chloroform. The nerves were cut and the peripheral ends ligatured separately. The left suprarenal gland was then excised by the lumbar route of operation. The peripheral ends of the splanchnic nerves were stimulated alternately with the same strength of faradic current (coil at 3,000 Kronecker, 5.4 volts current).

The following table gives an account of the consecutive procedures.

TABLE III.

| Chloroform | Splanchnic Stimulation    | Pulse Rate         |                   | Heart rhythm.                                |
|------------|---------------------------|--------------------|-------------------|--|
|            |                           | before stimulation | after stimulation |  |
| 0.6%       | Left                      | 120                | 120               | Regular before and after stimulation.        |
| 0.6%       | Right                     | 120                | 180               | Regular before, irregular after stimulation. |
| 0.6%       | Right                     | 120                | 240               | Regular before, irregular after stimulation. |
| 0.8%       | Right suprarenal excised. |                    |                   |  |
| 0.8%       | Left                      | 150                | 150               | Regular before and after stimulation.        |
| 0.8%       | Right                     | 135                | 135               | Regular before and after stimulation.        |

This experiment is illustrated in Fig. 14; it affords evidence that a nervous influence will stimulate a suprarenal body to secrete sufficient adrenalin to excite a typical ventricular tachycardia under chloroform. The occurrence of irregularities in an animal subjected to such extensive dissection is especially significant, and it may be taken therefore as certain that the irregularities previously observed on stimulation of the peripheral end of a cut splanchnic nerve were in reality conditioned by the enhanced secretory activity of the suprarenal bodies, and that it is unnecessary to consider the co-existing pressor effect in this relation. So also an explanation is afforded of the reflex cardiac reaction from sensory stimulation in animals deprived of their stellate ganglia; the reaction cannot be a direct reflex nervous action on the heart, but the heart is affected through the extra adrenalin secreted by reason of the reflex sympathetic stimulation of the suprarenal bodies. This reflex secretory effect has been directly demonstrated in other ways by Elliott and by von Anrep.

Having established the foregoing point it became necessary to re-investigate the function of the accelerator mechanism when excited by sensory excitation after excluding the adjuvant action of suprarenal secretion.

Attempts were made to isolate the suprarenal bodies from nervous influences by severing their splanchnic nerve supply, but, as I was never quite satisfied that all the sympathetic connections were dealt with, I preferred to rely only on experiments in which both glands had been extirpated. Five experiments were performed in which both glands were removed; in two of these excitation of the sciatic nerve, both by cutting and by faradic excitation, produced ventricular irregularity of a moderately high grade, the highest pulse rates noted being 240 and 270 respectively. In the three other cats the splanchnic nerve was stimulated in continuity; in one very little change in the beat was produced, in the second the heart was exhibiting a tachycardia from the commencement and hence the results were obscured; in the third cat the heart was likewise irregular from the first, and in this case a strong splanchnic stimulation (coil at 30 mm.) sent up the rate of beat from 225 to 300 per min. and caused permanent ventricular fibrillation in 20 seconds.

In order to avoid the fatigue and shock of the double operation, in one other cat the right suprarenal was previously extirpated, the left gland alone being removed at the time of the experiment. This experiment is illustrated in Fig. 15 and described as follows:—

*Experiment, 18/1/13.* Left suprarenal extirpated on 3/1/13. Right suprarenal excised and right sciatic cut under 1.7% chloroform.

TABLE IV.

| CHLOROFORM. | STIMULATION<br>COIL AT | HEART BEAT              |                                   |
|-------------|------------------------|-------------------------|-----------------------------------|
|             |                        | BEFORE STIMULATION.     | AFTER STIMULATION.                |
| 1.7%        | 90 mm.                 | 130 per min., regular   | 140 per min., regular.            |
| 0.5%        | 90 mm.                 | 180 per min., regular   | 280 per min., irregular.          |
| 0.5%        | 50 mm.                 | 240 per min., irregular | 300 per min., V.F. in 20 seconds. |

It is thus certain that all the reflex cardiac effects produced in the intact animal by sensory stimulation may be reproduced in an animal deprived of its suprarenal glands, that is to say, the reflex is equally active apart from any adjuvant secretory activity of the suprarenal glands. Thus, in the absence of any other unrecognised factor, sensory stimulations under chloroform may be said to effect the onset of cardiac irregularities by a dual agency; *i.e.* (1) by reflex stimulation of the heart through the cardiac nerves, (2) by reflex stimulation of the suprarenal glands. Possibly both of these factors are capable of producing ventricular fibrillation individually, and it is difficult to say which plays the greater part; it is known, however, that direct excitation of the cardiac nerves is far more potent in this respect than stimulation of the splanchnic nerves, and it may be inferred therefore that the former is the more frequent actual determining cause of complete ventricular fibrillation from reflex stimuli.



If sensory-cardiac reflexes under chloroform operate along these two paths alone, then no irregularities should appear on exciting a sensory nerve in cats in which both accelerator and suprarenal influences have been excluded. Such experiments have been attempted, but present considerable technical difficulties; in the first place the stellate ganglia must be excised and the animals allowed to recover; at a subsequent operation the suprarenal influence is cut off, and the animal again allowed to recover. When quite strong again, the experiment is performed. In one series of experiments of this nature I severed the splanchnic nerves on both sides at the second operation, and any obvious and accessible supplementary rami of the

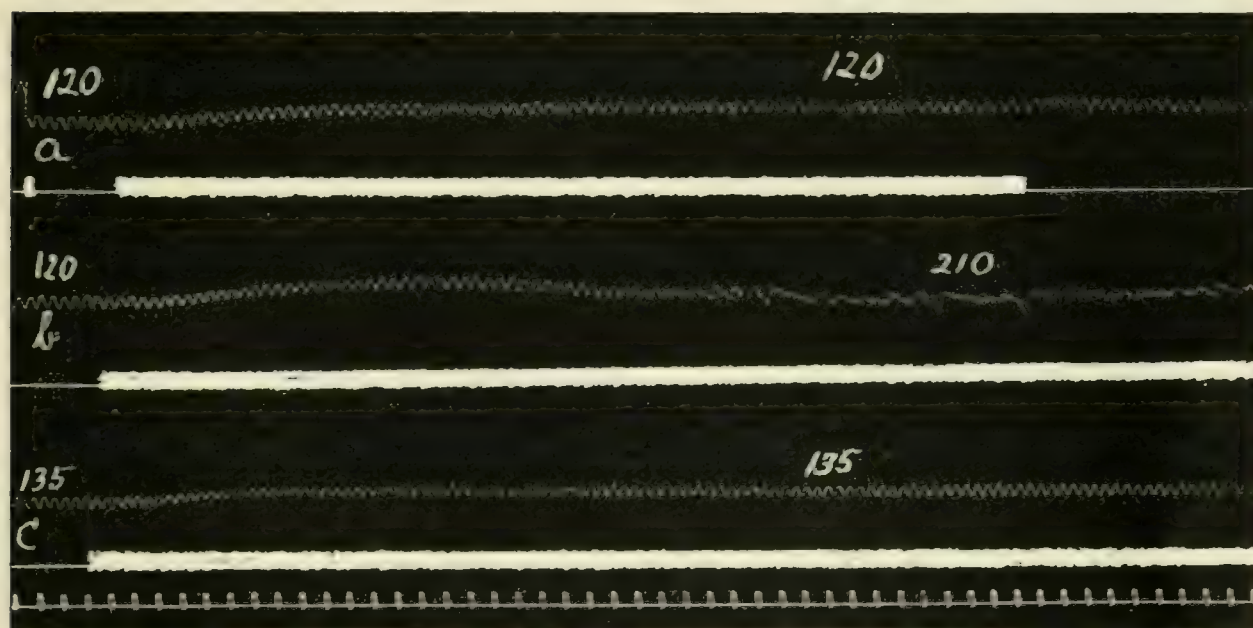


Fig. 14.  $\times \frac{2}{3}$ . Stimulation of the peripheral ends of cut splanchnic nerves. Coil at 3,000 Kronecker, 5.4 volts. Hürtle manometer.

A. Chloroform 0.5%. Left suprarenal extirpated, left splanchnic stimulated. The blood-pressure rises from vasoconstriction, but the heart beat is unaffected.

B. Chloroform 0.5%. Right suprarenal *in situ*, right splanchnic stimulated. The heart passes into an irregular tachycardia from increased secretory activity of the right suprarenal body.

C. Chloroform 0.8%. Right suprarenal extirpated, stimulation of the right splanchnic nerve. As in curve (a) the heart is now unaffected. The signal line in each case adjusted as abscissa. Time marked in seconds. The numbers above the curves indicate rate of heart beat. The splanchnic nerves had been exposed in the thorax and the respiration maintained by artificial means.

sympathetic system passing to the semilunar ganglia or suprarenals. In nearly all these experiments I obtained an actively irregular condition of the heart from sensory stimulations, but, as I have already observed, such a method of isolating the suprarenals is unsatisfactory—in fact, I invariably found at the *post-mortem* examination some accessory fibres which came off below the splanchnics, or even a splanchnic branch, remaining uncut; in view of the extensive nervous plexus (Reighard and Jennings<sup>24</sup>) around the suprarenals the possibility of a reflex secretory effect could not be excluded with certainty.

In two further cats, therefore, I adopted the method of excising the suprarenals themselves ; this was done in two stages, as described in a former relation, and in both these instances distinct acceleration and irregularities were caused by stimulations of a sciatic nerve, and this both before and after section of the vagi. In both of these cases, however, groups of ganglion cells were subsequently found in the regenerated tissues at the seat of the operation for excision of the stellate ganglia, and in view of this fact I think it is inadvisable to draw any definite conclusions or even to discuss these experiments until they have been more completely confirmed or negatived.\*

Apart from all theoretical consideration of these lines of action a matter of outstanding practical importance has been conclusively demonstrated in this section, viz., *that a sensory stimulation under light chloroform anæsthesia may, through one or more reflex mechanisms, throw the ventricles of the heart into a condition of permanent and fatal fibrillation, or may initiate irregularities which may terminate later in ventricular fibrillation. Under fully established chloroform anæsthesia such an event never happens.*

(b) *Reflex cardiac syncope in the chloroformed human subject.*

It cannot be doubted that a similar reaction to that described above may occur in the human subject. The adrenalin tachycardias and death occur in the chloroformed human subject, and there is no reason to question that man is similarly sensitive to sensory stimulations. The annals of fatalities under chloroform teem with references to sudden and fatal syncope on the first touch of the surgeon's knife or during the earliest stages of an operation, just as the more intense effects are more readily obtained experimentally in recently anæsthetised and vigorous animals. A large proportion of these fatalities occur in the course of trivial operations under chloroform in which, to save unnecessary subsequent discomfort, the minimum amount of chloroform is administered.

Unfortunately there are few absolutely precise records of the events accompanying death under chloroform in man ; naturally this is not a fitting moment for making scientific notes of pulse and respiration, and accounts written subsequently are generally confused, especially in regard to the time relation of events. Here and there, however, clear descriptions may be found ; to illustrate my point I will confine myself to a single striking case described by Dr. Alex. Wilson, Senior Anæsthetist to the Manchester Royal Infirmary :—

*CASE 6.* The patient, a girl of fifteen years of age, was operated on for *genu valgum* by Macewen's method. Chloroform was given on lint ; she took it well, the operation was performed, and the splint in process of being put on. At this stage, under the impression that all painful operative procedures were completed, the anæsthetic was discontinued. The patient was then breathing quietly ; she had a good pulse and normal colour ; the pupils were slightly contracted, and the corneal reflex was present—in fact, she was coming out of the anæsthetic, but was *sufficiently insensible to bear ordinary manipulations or even incisions without feeling pain*, and

---

\* The possibility of a reflex stimulation of the pituitary body may be taken into consideration ; for the extract of this gland is capable of exciting ventricular irregularities.



was as well as anyone could wish her to be. At this instant the surgeon suddenly forcibly flexed the left knee, which was stiff owing to osteotomy having been performed on that side a few weeks previously. The adhesions gave way easily with a crunching sound, and the patient uttered a scarcely articulate cry, immediately became deadly pale, and began to breathe deeply. She passed at once into the following condition: The head was turned to one side, the face was deadly pale, the eyes were slightly open, the pupils were widely dilated, and she was taking deep inspirations, the air passing freely into the chest; the muscles of the *alae nasi* were also acting, and the pulse was imperceptible at the wrist. The symptoms conveyed the impression that she had fainted. To drop the head, elevate the limbs, and apply hot sponges, &c., were the work of a moment. She continued to make strong respiratory efforts, and air was freely entering the lungs, but there was still no sign of the radial pulse. It appeared at first that the patient would probably recover—it seemed impossible that she could die with such active respiration; but the breathing, without shading off in the least, suddenly ceased, and every effort to restore life failed. (*Lancet*, 1894, II, 1148.)

I have selected this illustration because it serves as a “type” case of ventricular fibrillation under chloroform from a reflex cardiac stimulation, corresponding in all essential details to those accompanying a death from cardiac stimulation by adrenalin in man and to those reflex syncope observed and described by me in animals. The essential features are very graphically portrayed, viz., the light anæsthesia, the sensory stimulation, the sudden and complete heart failure, the continued and deepened respirations and the ultimate respiratory failure. It is not in every case of death from ventricular fibrillation that the attendant conditions are so well defined, or at least so carefully observed, and, in fact, under special conditions the special features are in some degree modified. A discussion of these modifications would be inappropriate in this paper: they require extended consideration and will be so considered from the clinical standpoint in a special paper bearing on this subject.\* I am content for the moment to present a case which clearly confirms the occurrence of a reflex cardiac syncope in the human subject and which affords a parallel with the similar deaths which I have induced experimentally in animals.

Can a death of this description be ascribed to any cause other than ventricular fibrillation?

It is absolutely certain that death in this particular instance was not conditioned by “over-dosage.” There remains the prevalent idea that sudden death may result from the reflex inhibition of the heart through the vagi, and this view was adopted by the author of this report. But no vestige of direct experimental evidence can be adduced in support of such a view, despite the innumerable attempts to produce a fatal vagal reaction in the chloroformed animal. Permanent inhibition of the mammalian heart by reflex vagal action is unknown to experimental physiology, and although it has been considered that vagal inhibition might be fatal to a diseased heart, this is a matter of pure conjecture.† I have myself made an extended investigation<sup>20</sup> upon this supposed reflex action of the vagus, and found that although well marked vagal effects may be obtained through stimulation of the central end of the recurrent laryngeal nerve or of fibres running in the

\* Two additional cases of cardiac syncope under known percentages of chloroform are given in the Appendix to this paper. (Nos. 1 and 2.)

† Certain clinicians are now employing vagal compression as a test in cases of heart affections; and they do so with impunity.



vagus trunk, yet even although the excitability of the vagus centre be raised by partial asphyxia, nothing approaching permanent stoppage of the heart's action is ever produced. I never observed any vagal reflex of practical significance as a result of stimulating sensory somatic nerves, and feel quite assured that no such thing ever happens, and it is evident that an *imagined* cause of death can no longer be accepted or even considered as an alternative to the *substantive* form of death through ventricular fibrillation which I have succeeded in demonstrating as a reflex phenomenon.

#### IV. THE DIRECT CARDIAC EFFECT OF SECTION OF THE VAGI.

Section of the vago-sympathetic trunks under light anæsthesia is one of the most effective measures for the production of typical chloroform

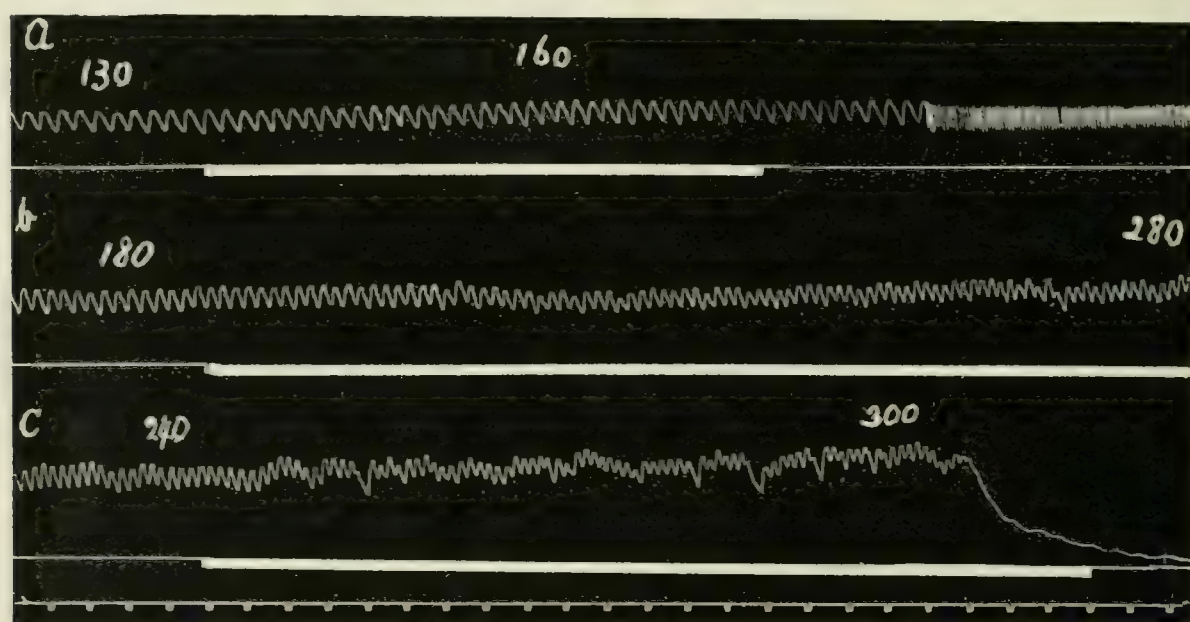


Fig. 15.  $\times \frac{2}{3}$ . Sciatic stimulations in a cat from which both suprarenal glands had been extirpated, the animal otherwise intact.

a. Chloroform 1.7%. Coil at 90 mm. The heart beat accelerates from 130 to 160 per minute, but remains regular.

b. Chloroform 0.5%. Coil at 90 mm. The heart beat passes into an irregular tachycardia, maximum rate 280.

c. Chloroform 0.5%. Stronger stimulation, coil at 50 mm. Heart irregular when stimulated. The irregularities become more pronounced and terminate in V.F. Hürtle curves. Signal lines adjusted as abscissa. Time in seconds. The numbers indicate rates of heart beat.

tachycardias. Under deep anæsthesia, produced by 2% vapour or over, it sometimes happens that the heart accelerates only, remaining perfectly regular, but under these circumstances also pronounced irregularities may occur. Under light anæsthesia the irregularities invariably occur in sequence to vagotomy. Sometimes these eventually disappear, the heart then remaining permanently accelerated but regular; sometimes they persist indefinitely, and in exceptional cases they terminate in ventricular fibrillation. These remarks apply to instances in which both vagi are cut; section of one vagus alone does not, as a rule, give rise to the more complicated forms of irregularities, often to a bigeminus only.



I have had frequent occasion to perform vagotomy upon cats under chloroform, not in order to induce irregularities, but for the purpose of control experiments, and an endeavour was therefore generally made to suppress the irregularities by maintaining a full degree of anæsthesia. In such cases the ventricles never passed into fibrillation. I have, however, in addition to these, seven records of cases in which vagotomy was performed at 1% or at a lower strength of vapour, and it is probable that there were a few other unrecorded instances in which there was a negative result. In these seven recorded instances the heart was beating regularly before the vagi was cut. In two instances at 0.0% and in three at 0.5% the usual multiple tachycardia alone ensued. In the two remaining instances definite ventricular fibrillation occurred, in one instance temporarily, in the other permanently.

*CASE 1.* Fig. 16. Cat under 1% chloroform. Rate of beat=90 per minute. Blood-pressure=102 mm. On section of one vagus the blood-pressure rose a little and the rate was slightly accelerated. On section of the contralateral vagus the blood-pressure rapidly rose to 120 mm. and the beat was accelerated to 150 per minute. The heart then became progressively irregular, and the blood-pressure fell owing to cardiac insufficiency. A series of simple forms of irregularity were the first to appear (bigeminal action) which passed into higher grades of irregularity with short intervals of fibrillation and later a well-marked temporary cessation of the heart's action towards the end of the tracing occurred.

*CASE 2.* Cat under 0.5% chloroform. Every fourth beat an extrasystole, rate about 90 per minute. Blood-pressure=100 mm. On cutting the vagi a multiple tachycardia ensued, the blood-pressure, after a preliminary fall on their first incidence, rising gradually to 146 mm. In 1½ minutes the ventricles passed into permanent fibrillation.

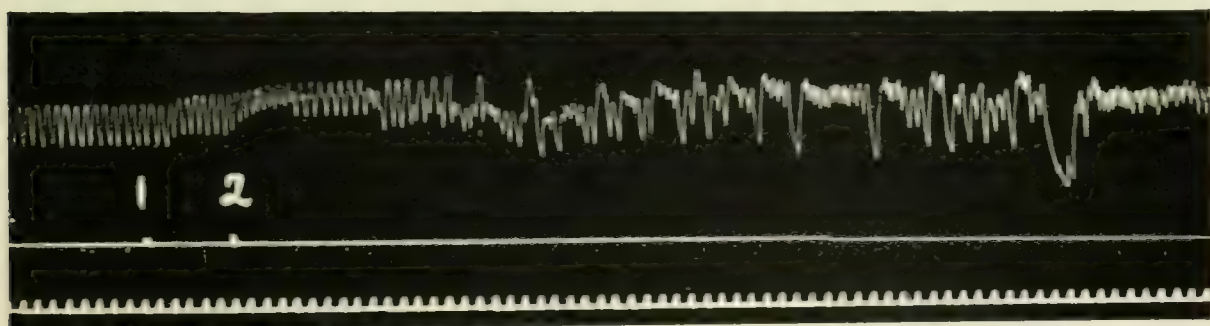


Fig. 16. Section of the vagi in a cat lightly anæsthetised by 0.5% chloroform. Previous to vagotomy the heart was beating regularly at a rate of 90 per minute. On cutting the vago-sympathetic nerve trunks in the neck (signal marks 1 and 2) the heart accelerates and the blood-pressure is forced up. The beat then by gradual stages becomes more and more irregular with momentary periods of ventricular fibrillation. Hürtle manometer. Natural respiration. Time marked in seconds. The signal line has been adjusted to the Hürtle abscissa.

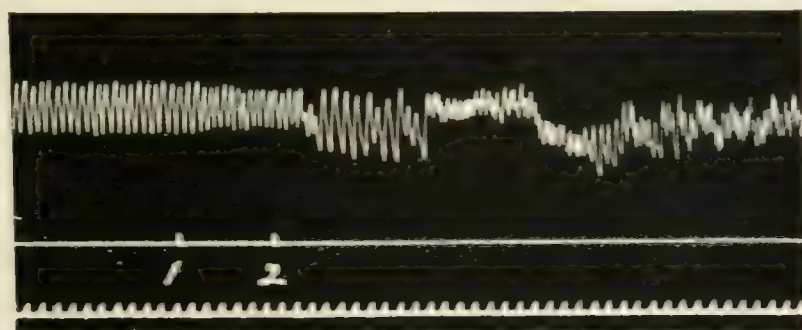


Fig. 16a. A similar experiment to the last, but in which the accelerator cardiac nerves were cut just previous to vagotomy. Chloroform 1.5%. Hürtle manometer.



The effect of exciting a vagus nerve is, as Gaskell<sup>7</sup> has shown, to depress all the cardiac functions. The effect of section of the vagus nerves is to cut out the tonic vagal influence on the heart, with the result of an increase in the cardiac functions, this increase being the equivalent of an excitation of the (so-called) accelerator nerves, which exert an exactly opposing influence to that of the vagi. Both section of the vagi and accelerator excitation, as is well known, increase the rate of rhythmic contraction of the heart, and also cause it to beat more strongly, so that the ventricular output is increased and the blood-pressure rises. These tendencies may be largely obscured under chloroform owing to the irritable condition of the heart and the consequent incidence of irregularities with loss of cardiac efficiency, but when observed apart from these abnormalities, the effect of section of the vagi is found to be precisely the same under chloroform as under other conditions. This fact is demonstrated under circumstances in which the heart is less irritable than usual, and in which as a consequence it remains regular after vagotomy, the manometric curve then presenting a perfect picture of increased cardiac efficiency. Thus :—

*Experiment, January the 6th, 1912. (Fig. 17). Cat under 1.5% chloroform, anæsthesia well established. Heart beat regular at a rate of 165 per minute. Blood-pressure = 98 mm. On section of both vagi the rate rapidly increased to 240 and the pressure rose to 144 mm. in 22 seconds. The beat remained regular.*

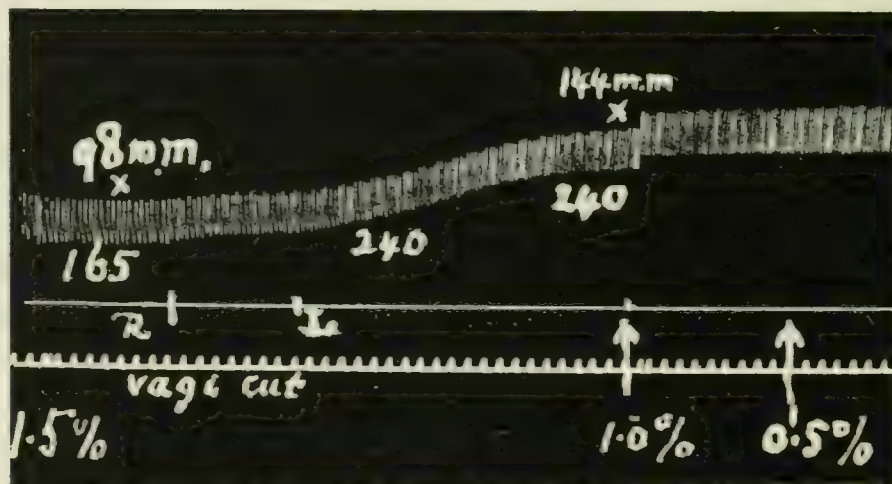


Fig. 17. Section of the vagi in a cat fully anæsthetised by 1.5% chloroform. The figures above the pressure curve indicate blood-pressure at the mark x, and those immediately below the curves denote rate of cardiac rhythm. The signal marks R and L denote section of the right and left vago-sympathetic nerve trunks respectively. The heart does not become irregular and hence the increased efficiency of the heart is fully represented by the rise of blood-pressure. A further rise takes place later as a result of reducing the anæsthetic at the arrow marks. Hürtle manometer. Signal line adjusted to serve as abscissa. Time marked in seconds.

A similar observation has been made on five other animals which were being subjected to artificial respiration, a condition which opposes the tendency of the heart to become irregular even in the presence of low percentages of chloroform. In these cases, likewise, on section of the vagi the heart remained regular but at once became accelerated, attaining generally a rate of 240 per minute or thereabouts. The blood-pressure was likewise affected, rising at once 10 or 20 mm., and subsequently and more gradually to a height which was in one instance as much as 50 mm. above the initial pressure.



The onset of ventricular irregularities as a consequence of vagal section may be explained in a manner which conforms with the explanations of my previously described experiments. Both adrenalin, and the so-called "accelerator" influences, whether direct or indirect, stimulate the heart to increased activity. By removing the tonic depressing influence of the vagal centres the heart is, in effect, *stimulated* in a precisely similar fashion. In short, it is a *stimulation* of the heart functions which is the determining cause of ventricular irregularities and fibrillation in a heart already rendered irritable by the action of chloroform.

► If the above conclusions be correct, then increased vagal activity should have the effect of abolishing existing tachycardias. This is undoubtedly the case. I have frequently excited the peripheral end of a cut vagus nerve and have thereby succeeded in putting an end to a ventricular tachycardia. Such an experiment is illustrated in Fig. 18.

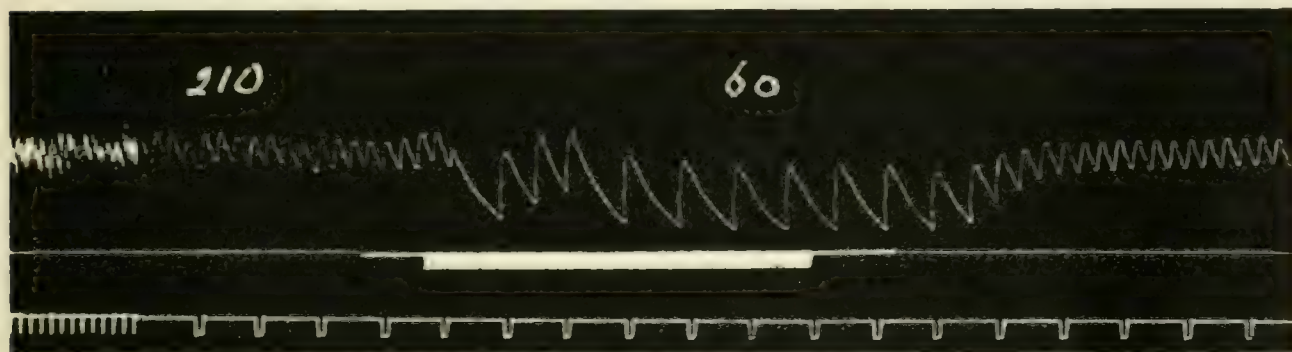


Fig. 18. The influence of vagal action upon the irregular heart. The peripheral end of a cut vagus nerve was stimulated by a faradic current with the coil at 90 mm. Before stimulation the heart was exhibiting an irregular tachycardia of 210 beats per minute. The irregular condition of the beat is more readily identified in that part of the tracing in which the kymograph moves at a slow rate. During excitation the heart is slowed to a regular beat of 60 per minute. Hürtle manometer. The signal line is adjusted to the abscissa. Time in seconds.

There is good reason to believe that an increase of vagal tone is responsible for a diminished liability to the *onset* of these cardiac irregularities, but I shall have occasion to deal with this point at greater length in my following paper.

A question of considerable interest is involved in the results of cutting the vagi. Does the cardiac stimulation and consequent irregularity arise as an automatic intracardiac increase of function, or does it arise from the now unrestrained, and hence augmented, action of the accelerator centres? This question appears to be fully answered by the following experiment:—

The cardiac accelerator nerves were exposed on both sides by Anderson's operation, and cut, and then the vagi were cut under 0.5% chloroform. The result was a procession of events almost exactly similar to that seen in Fig. 16, the heart passing by similar stages into a multiple tachycardia. (See Fig. 16a.) This result was confirmed in a later series of experiments on cats with denervated hearts, *i.e.*, on surviving cats in which the stellate ganglia

had been excised. The denervated heart is possibly even more sensitive than the normal heart, and in this series of nine experiments I met with a case of ventricular fibrillation from vagotomy under the exceptional condition of a 2% chloroform anæsthesia. Another case fibrillated under 1% chloroform vapour, and in the remaining seven the usual irregularities alone resulted. In these experiments the possibility of an exaggeration of the normal accelerator tone is excluded, and one is therefore led to conclude that ventricular abnormalities following section of the vagi under chloroform are not directly excited by a nervous impulse, but occur in sequence to a stimulation of the heart which is not the result of a direct nervous influence. In other words, the seat of origin of excitation of ventricular fibrillation after section of the vagi is intracardiac, and presumably, intramuscular.

The possibility of traumatic irritation (due to section) of afferent vagal fibres setting up a secretory reflex in the suprarenal bodies, and thus conditioning the irregularities in the foregoing experiments, may perhaps be considered. These afferent fibres are largely cardio-inhibitory and vasodilator in action, and such effects alone, so far as I have observed, result from the faradic excitation of the central ends of the severed vagi. It can, farther, be demonstrated that vagotomy gives rise to the same irregularities after excision of the suprarenal glands in addition to the stellate ganglia, and thus additional support is afforded to the view that they are purely intracardiac in origin. The following experiment illustrates this point:—

*Experiment.* Cat. Stellate ganglia excised seventeen days previously. Animal in fair condition. Both suprarenal glands excised, heart-beat regular, 120 per minute. The vagi were then cut under 1% chloroform and cardiac irregularities followed in twenty seconds.

Section of the vagi is an experiment which has no direct clinical counterpart. There does, however, exist a possible physiological parallel in a diminution of the normal vagal tone through reflex inhibition of the vagus centres, a subject which has been considered at some length by Reid Hunt.<sup>10</sup> Whether this may be an adjuvant cause of ventricular irregularities I cannot say, but inasmuch as I have obtained positive results in all my control experiments with the vagi previously cut, it does not appear to be a matter deserving immediate further investigation.

#### V. VENTRICULAR FIBRILLATION OF APPARENTLY SPONTANEOUS ORIGIN.

In the foregoing section I have described how reflex stimulation of the heart, such as results from operative procedures, may produce ventricular fibrillation under conditions of light chloroform anæsthesia. I have now to describe how ventricular fibrillation likewise occurs (1) during the induction stage, when the heart has not come fully under the influence of the chloroform, and (2) during the recovery stage, when the heart is being released from the full influence of the chloroform. In these stages ventricular fibrillation may be apparently spontaneous in origin, in so far as there is not any source of reflex cardiac stimulation arising from operative manipulations.





Fig. 19.  $\times \frac{3}{4}$ . Ventricular fibrillation-caused by struggling during the induction period. Cat prepared by Brooks' method. Cannula in crural artery. Upper curve, respiratory. This shows a declination in its first portion caused by a leak in the recording apparatus. Lower curve, blood-pressure. Ludwig manometer.

Anæsthesia induced by 1.5% chloroform, then 2%, then reversion to 1%, when animal was roused to a state of excitement and struggled freely. The heart became very irregular, the chloroform was entirely removed, and the ventricles fibrillated a few seconds later. The fluctuations in the blood-pressure during struggling are mainly mechanical, and the small irregular beats are almost obscured in the reproduction. The final fluctuations at the foot of the pressure curve are caused by the powerful asphyxial respiratory gasps, which are delineated in the respiration curve. The heart was inspected immediately on the cessation of respiration. The ventricles were found in a state of coarse fibrillation. The auricles were beating faintly, the left auricle containing blood which was darker than usual after V.F.

(a) *Observations without recording apparatus.*

A brief account of ventricular fibrillation occurring in the induction stage of chloroform anæsthesia in cats, and of the definite ways in which it is brought about, has already been published.<sup>15</sup> Eighteen cases of sudden death during the induction of anæsthesia had been noted at the time, and several more of an exactly similar nature have been since observed. Many of these cases were the result of a pure accident at a time when I was unaware of the proper principles of administration, and others more recently have been the result of set procedures in the endeavour to reproduce them. These deaths are of a remarkably sudden nature, the animal is obviously not overdosed, yet the respiration stops suddenly from no apparent cause, the heart is found to have ceased beating and in the generality of cases no measures, however prompt or energetic, will avail to restore the animal.

If the animal were being carefully observed shortly before the respirations ceased a phase of exaggerated respiration would be noted, often of itself sufficient to attract attention, and sometimes taking the form of powerful expiratory spasms, accompanied by loud phonation, the whole body at the same time twisting in a convulsion. Sometimes violent struggling, evidently the volitional efforts of a semi-conscious animal, would precede the terminal phase of exaggerated respiration. This form of death in animals has been recognised and even carefully described, and the cause of

death ascribed to an excessive intake of chloroform as a result of the abnormal respiratory amplitude. There is an element of unconscious irony in this attempt to exploit a physiological theory upon the body of a dead animal, for the animal is indubitably dead before the exaggerated respirations appear; they are but the physiological sequence of a rapid and complete circulatory failure, to which reference has already been made in Section I (a) of this paper (see Fig. 19). These asphyxial gasps are an almost invariable sequence of ventricular fibrillation from any cause, but in some cases they are modified by the condition of the animal or the degree of anæsthesia; thus the respirations, though continuing after cardiac syncope, may not be exaggerated, or they may even, though long drawn, be diminished in amplitude.

Although when, some years ago, I first observed this form of death I did not recognise its cause, I was convinced it did not result from an excess of vapour. The anæsthesia was at that time induced by placing a bag made of loosely woven fabric on the animal's muzzle and dropping chloroform upon it. The process was carried out with precision and with a careful progression so that I was in this way enabled to chloroform cats without any excitement and without any assistance and to avoid over-dosage with certainty. From my knowledge of the evaporation of chloroform under such conditions I was convinced that at no stage was an excessive percentage of chloroform administered.

At a later stage I induced anæsthesia by means of the bag and drop bottle, and discarding this when the animal was fairly anæsthetised I continued with the *ad plenum* method of administration with a 2% or lower strength of vapour. An interval, during which the cat was not inhaling an anæsthetic, was thus introduced.

Subsequently anæsthesia was habitually induced from the beginning by the *ad plenum* method, commencing with a low percentage and gradually increasing it, but the administration was not always continuous, the inhaler being sometimes removed to examine the corneal reflex or for other purposes. In the course of the pursuance of this method, the percentages being noted throughout, the same form of death was seen, thus affording definite and final proof that the percentage was within the so-called limit of safety, viz., 2%.

At first there was no suspicion of ventricular fibrillation as a cause of death in these cases; when this was suspected later, evidence of it was sought for by opening up the chest and pericardium. When this was performed immediately after syncope the evidence was unmistakeable, but on the other hand if the *post-mortem* was delayed for purposes of attempting the recovery of the animal, then the evidence might be presumptive evidence only, for actual fibrillar contractions might have passed away, but even under such circumstances the absolute inactivity of the ventricles is a suggestive feature. The determining causes of death were not at first apparent, but it became progressively evident that an entire withdrawal or great reduction of the chloroform was a factor of outstanding importance



in the procedure, and such a factor is specifically noted in nearly all my notes of the cases. I am now able to classify the procedures which may lead to syncope under three headings :—

1. On intermitting the administration. On taking off the chloroform the animal dies spontaneously, with or without signs of recovery (*i.e.*, movement, &c.) from the anæsthetic.

2. On struggling. After stopping the administration, or when under a low percentage, the animal was caused to struggle, frequently as a result of tying it down on the experimental table. This struggling precipitated spontaneous syncope.

3. On increasing the chloroform suddenly or on re-applying it after an intermission. On the animal showing signs of recovery either by struggling or by minor evidences, more chloroform was given, and this re-application was quickly followed by syncope.

A complete account of the cases of syncope upon which the above conclusions are founded is given below in chronological order. The descriptions are given just as they were noted at the time. Unfortunately these notes are not in every case very complete, being, many of them, made at a time when the significance of all the circumstances was not fully appreciated.

*List of cases of syncope during the induction of chloroform anæsthesia.*

| CASES.   | CAUSE OF SYNCOPE.                |
|--|----------------------------------|
| <p>1. May the 22nd, 1908. Drop method.<br/>Cat came round a little and moved about before tying down on board. Some extra chloroform given when tied down. Gave several strong gasps and found to be dead. No recovery by artificial respiration or on prolonged perfusion.<br/>No P.M.</p>  | Intermission and re-application. |
| <p>2. May the 29th, 1908. Drop method.<br/>Took some time to go under. Made quite flaccid and quiescent and tied down to board, chloroform kept up as before. When tied down struggled pretty violently, about 10 drops quickly applied to the nose bag. Almost immediately after found not breathing and heart not beating.<br/>A few gasps, but no sign of heart action afterwards in spite of artificial respiration.<br/>No P.M.</p> | Struggling and re-application.   |
| <p>3. September the 12th, 1908. Drop method.<br/>When tied down on board struggled and phonated, five drops put on nose bag, within a few seconds the breathing and pulse stopped . . . . . Breathing and pulse gradually recovered.<br/>Recovery.</p>   | Struggling and re-application.   |

| CASES.  | CAUSE OF SYNCOPE.   |
|---|---|
| <p>4. September the 28th, 1908. Drop method.</p> <p>One out of eight cats in which an attempt was made to reproduce this form of death. Struggled very strongly during induction. When it had not had more than three drops at a time it commenced to inflate its chest deeply and respire powerfully apparently against a partly closed glottis, the cat being held by the legs at the time. The heart beat was not readily perceptible, as the chest wall was very tense. Five drops then put on nose bag, breathing quieted down, heart beat still not readily felt, when tail spasm was noted and breathing suddenly ceased. Attempted recovery by chest compression and tongue traction. Cat gave about six gasps at intervals, but the heart never recovered and normal breathing never reassumed.</p> <p>No P.M.</p> | <p>Probably V.F. from struggling, followed by recovery, with relapse on re-application.</p> |
| <p>5. December the 1st, 1908. Drop method.</p> <p>Three to five drops rather rapidly repeated. Went slack early when the heart noticed to be beating very faintly, respiration good. Chloroform discontinued, and the animal tied down when it very quickly came round with a quite strong and slow heart beat. As far as can be remembered two doses of five drops each were then applied. Heart beats soon noticed to be imperceptible, respirations remaining regular and fairly vigorous. Chloroform removed, but breathing gradually failed and animal restored with great difficulty by chest compression and tongue traction. Many gasping respirations occurred before the heart commenced to beat again. Recovery.</p>   | <p>Intermission and re-application.</p>   |
| <p>6. May the 17th, 1909. Drop method.</p> <p>Chloroform applied carelessly in large amounts, heart felt to be faint early in administration. Chloroform removed. The corneal reflex was very active and animal moving when it became convulsed strongly on applying a fresh dose, and then heart beat was found absent and breathing ceased. Breathing was restored actively but not the heart.</p> <p>No P.M.</p>   | <p>Intermission and re-application.</p>   |
| <p>7. August the 15th, 1910. Drop method followed by <i>ad plenum</i>.</p> <p>Put under thoroughly by drop method with the intention of continuing by <i>ad plenum</i> method. The apparatus was found not to be working properly, so decided to abandon experiment and nose bag removed. The apparatus was quickly mended however, and experiment resumed, animal now coming round and moving slightly. Given 2% <i>ad plenum</i> and proceeded to tie down. When tied down animal found dead and could not recover it. Judging by the want of resistance on tying down the cat expired almost immediately on giving 2%.</p> <p>P.M. Heart exposed. Auricles beating, ventricles not beating. Right ventricle fibrillating very finely at one spot near apex, later fibrillation became more evident generally.</p>        | <p>Intermission and re-application.</p>   |
| <p>8. September the 14th, 1910. Drop method followed by <i>ad plenum</i>.</p> <p>Chloroform rather pushed, went under readily. Became quite slack and breathing became weak, heart slow but quite palpable, corneal reflex still active. Nose bag taken off and then continued with 2% <i>ad plenum</i> method. Soon commenced to struggle and breathe deeply and within thirty seconds became motionless, no heart beat felt, breathing stopped. A few breaths induced by tongue traction, but heart never beat again.</p> <p>No P.M.</p>  | <p>Intermission, re-application and struggling.</p>   |



| CASES.  | CAUSE OF SYNCOPE.  |
|---|--|
| <p>9. November the 9th, 1910. <i>Ad plenum</i> method.</p> <p>Put under by <i>ad plenum</i> method gradually increasing vapour up to 2%, then back to 1.5%. Incision made in neck, struggled, put chloroform up to 1.8%, incision continued, struggled again and the funnel slipped off the head. Left under chloroform again whilst attention diverted, then noted breathing stopped and heart not going. Breathing recommenced spasmodically for a short time, but heart never recovered.</p> <p>P.M. Heart distended. Auricles beating rapidly. Right ventricle fibrillating slightly. Left ventricle faint fibrillation later.</p>  | <p>Struggling, intermission and re-application.</p>                    |
| <p>10. December the 3rd, 1910. <i>Ad plenum</i> method.</p> <p>Induction first with 1%, then with 2%. When fully relaxed tied down. Breathing noticed rapid but very shallow, heart beating rapidly but strongly. Percentage reduced to 1.8% when animal suddenly went into a general spasm, commencing in the tail, fully inflated chest which became very tense. Spasm lasted a few seconds and at the end of it the heart found not beating. All efforts at recovery unavailing.</p> <p>No. P.M.</p>   | <p>Intermission (not noted but almost certain) and re-application.</p> |
| <p>11. December the 6th, 1910. Drop method.</p> <p>Cat sneezed and blew the bag off its muzzle when half way under. Bag re-applied, struggled a little, then two or three drops put on and heart found to have stopped almost immediately afterwards. Natural breathing recurred spasmodically, but heart beat never returned. Vagi were cut without result.</p> <p>P.M. Chest opened late. Ventricles quite inactive, did not show any signs of fibrillation; auricles only beating feebly.</p>  | <p>Intermission and re-application.</p>                                |
| <p>12. December the 13th, 1910. Drop method.</p> <p>Gradual induction. Heart beat rapid but not strong. Sneezed violently, chloroform continued during sneezing, not in excess. Cat then gave several expiratory groans, chest strongly inflated several times and then collapsed dead.</p> <p>Vagi cut and other methods of restoration tried without avail.</p> <p>P.M. Chest opened late. Ventricles quite inactive and not fibrillating. Heart not over-distended. Auricles beating extremely feebly and at long intervals.</p>   | <p>Sneezing and re-application.</p>                                    |
| <p>13. December the 13th, 1910. Drop method followed by <i>ad plenum</i>.</p> <p>Chloroform given fairly rapidly. When apparently well under took off nose bag. Cat sneezed a little and 2% given through funnel. Sudden collapse followed, no recovery.</p> <p>No P.M.</p>   | <p>Intermission and re-application.</p>                                |
| <p>14. February the 24th, 1911. <i>Ad plenum</i> method.</p> <p>2% from beginning. Rapid heart beat. Quiet for first two minutes of induction, then commenced to sneeze, inhaler removed for about thirty seconds, corneal reflex active. Inhaler re-applied when sneezing had ceased. Amplitude of thoracic respirations almost immediately increased, inflated chest with expiratory groans, heart could not be palpated on account of the tense chest walls. When respiration ceased, as it did quickly, heart beat could not be felt. At the moment of re-application the inhaler was yielding exactly 1.9% vapour.</p> <p>P.M. Chest opened at once. Ventricles fibrillating. Right auricle fibrillating very evidently, left auricle beating rapidly.</p> | <p>Intermission and re-application.</p>                                |

| CASES.   | CAUSE OF SYNCOPÉ.                   |
|--|-------------------------------------|
| <p>15. March the 2nd, 1911. Induction <i>ad plenum</i>, 2% from the beginning.</p> <p>Incision in neck made when under, and reduced chloroform to 1.5%. Commenced to struggle violently and chloroform raised to 2%, but previous to this the respirations were increased in a typical manner, with rigidity, so that the heart could not be palpated. No doubt the heart stoppage occurred before the chloroform was increased. P.M. Chest opened some time after. Ventricles fibrillating finely, fibrillation increased by massage. Auricles beating.</p>   | Struggling.                         |
| <p>16. Date ? Drop method.</p> <p>Came round on tying down. A few more drops induced forced respirations and death.</p> <p>No P.M.</p>   | Re-application.                     |
| <p>17. August the 2nd, 1912. <i>Ad plenum</i> method.</p> <p>2% chloroform <i>ad plenum</i>, for three minutes, breathing quite quietly, not deeply under at any time, heart beating quietly, not fast, corneal reflex present not very active. At the end of three minutes chloroform removed as an intentional test, respiration increased in force almost at once, no struggling, phonated, and breathed deeply. No heart beat felt when spasm of chest had passed off.</p> <p>P.M. Ventricles fibrillating; right auricle fibrillating faintly, left auricle beating faintly. Right auricle purple, left auricle bright red.</p> | Intermission.                       |
| <p>18. August the 2nd, 1912. <i>Ad plenum</i> method.</p> <p>2% given for about two minutes. The delivery tube to the funnel then became kinked, causing an intermission of the vapour. Phonation, deep breathing and death. No movement or struggling.</p> <p>No P.M.</p>   | Intermission.                       |
| <p>19. September the 22nd, 1912. <i>Ad plenum</i> method.</p> <p>(Attempt to kill by chloroform in a series of six cats.)</p> <p>Cat 5. Cut male. 2,128 grms. Had plenty of milk and meat up to evening of 21st, but nothing since.</p> <p>2.46 p.m. 1% on. <i>Ad plenum</i>.</p> <p>2.50 p.m. 1% off. Heart beat fairly if not quite regular at first. Sneezed once and looked round, no other movement. In about twenty seconds the heart beat was felt to cease suddenly, increased respiration immediately followed.</p> <p>No P.M.</p>  | Intermission.                       |
| <p>Cat 6. Cut male. 2,455 grms.</p> <p>Fed as No. 5.</p> <p>2.59 p.m. 1% <i>ad plenum</i>, on.</p> <p>3.3 Spasmodic movement and phonation.</p> <p>3.3½ Struggling. Chloroform off, heart becomes irregular.</p> <p>3.4½ 1% on.</p> <p>3.6½ Struggles strongly. Heart suddenly ceased beating, respiratory spasm and loud phonation ensuing.</p> <p>3% put on with later gasps, when heart recovered permanently.</p> <p>Recovery.</p>   | Struggling during light anæsthesia. |
| <p>20. January the 14th, 1913.</p> <p>Cat put deeply under by unmeasured chloroform vapour in a cup. This induced at first violent struggling and an intense persistent tachycardia. When under, cup taken away, and after a brief interval <i>ad plenum</i> method with 2% vapour substituted. Death almost immediately with usual symptoms.</p> <p>No P.M.</p>   | Intermission and re-application.    |



The foregoing account of twenty-one deaths, occurring during the induction of chloroform anæsthesia in cats, sheds an entirely new light upon the conditions of dosage under which they die in this stage of the administration of chloroform. In those cases in which the chloroform vapour was supplied in measured concentrations the factor of overdosage can be excluded with certainty; in many of those cases in which the chloroform was not mechanically regulated, it was administered in such restricted quantities as to exclude the factor of overdose with practical certainty. The condition of the animals in relation to their low dosage may be further judged by the fact that some of them were moving slightly or struggling, and some were in fact in a state of semi-consciousness at the moment preceding the final collapse. Finally when the cats died as a result of the re-application of the vapour the short space of time which elapsed between the re-application and the syncope, the frequently instantaneous sequence, entirely precludes all possibility of a sufficient intake of chloroform to oversaturate the tissues.

When an animal is overdosed with chloroform the respiratory and cardiac phenomena are entirely different from those described above. The respirations gradually become weaker and then fail; they do not become exaggerated or fail suddenly. The heart beat persists after the failure of respiration, and even if not palpable, at least the ventricles may be seen, on inspection of the heart, to exhibit a feeble, but rhythmical, beat for some minutes after respiratory failure; both auricles are seen to be purple in colour as a result of their both containing venous blood; the *post-mortem* appearance of the overdosed heart is thus sufficiently distinctive. After respiratory failure such as that caused by an excessive administration of chloroform, the animal can be resuscitated readily enough by ordinary means; in support of this assertion I may cite the authority of Snow<sup>27</sup> and Paul Bert,<sup>1</sup> who employed vapours up to 6% strength, and this view is, I think, generally accepted. In the majority of my cases the heart did not recover spontaneously, nor could it be restored by any of the methods usually employed for the purpose of resuscitation.

My cats therefore did not die from overdosage; this is demonstrated by—

1. the restriction of vapour;
2. the evidences of light anæsthesia;
3. the mode of respiratory and cardiac syncope;
4. their insusceptibility to resuscitation;
5. the *post-mortem* appearance of the heart.

Any one of these reasons is in itself convincing; taken in conjunction they constitute overwhelming evidence of the truth of my conclusion.\*

The symptoms accompanying the syncope were in all these cases compatible with primary cardiac failure from ventricular fibrillation, a

---

\* In two cases (Nos. 11 and 12) the vagi were cut after death without result. The syncope was therefore not due to Embley's form of vagal cardiac inhibition.

condition which I have shown to be fostered by *light* chloroform anæsthesia, and a condition which was demonstrated in certain instances after death.

As the result of the foregoing observations and considerations I adopted a certain definite plan of administration—I induced anæsthesia more rapidly by giving the animal a fairly full percentage of vapour, 2% or more, to inhale from the commencement. The administration was made a perfectly *continuous* one, never on any account intermitted, and the strength of the vapour never reduced; if the animal struggled it was firmly restrained, and the struggles were not allowed to interrupt the administration. I have now had an experience of some 300 cases of chloroform anæsthesia induced by this method, with a single instance of death (No. 18), and this death followed the accidental interruption of the administration through a rubber supply tube becoming temporarily obstructed. This experience lends further confirmation to my views regarding the cause of death, for it is in striking contrast to that appertaining to the usual intermitted method of administration in common use, and which has led to the disuse of chloroform as an anæsthetic in many physiological laboratories. Briefly related, it may be said that anæsthesia may be induced with perfect safety with chloroform, provided it is given *of a full strength and in a perfectly continuous manner*.

The occurrence of a death as a simple sequence to removing chloroform occurred in only three of the related twenty-one cases of death, but this occurrence is more frequently met with after the conclusion of an operation under aseptic conditions, such, for instance, as excision of the stellate ganglia, performed with the object of allowing the cat to survive; this fatal conclusion is indeed so frequent that I never now use chloroform for these aseptic operations. This death on recovery seems to be more favourably conditioned by a somewhat prolonged preliminary subjection of the heart to the action of chloroform at a moderate percentage strength; deep and prolonged narcosis tends to abolish the risk. The syncope may occur within a few minutes of the termination of the operation, or it may be delayed for an hour or more; it may occur in a perfectly quiescent animal, but is more usually preceded by some form of unconscious movement or by a fit of general excitement. The symptoms of this death on recovery are precisely similar to those described as occurring on intermission of the vapour during induction, and the cause of death is made apparent by laying open the chest and inspecting the heart.

*Illustrative case.* (August the 2nd, 1911.) Cat. Induction with 2% chloroform, *ad plenum* method. When under, the chloroform was reduced to 1.5% whilst the neck was being shaved. The chloroform was then taken off and a bandage rolled round the neck, and then the animal was laid on its side on a bench to recover. A few minutes later the cat commenced the “running” movements which are so frequently a sign of returning consciousness. These movements ceased suddenly within a few seconds of their appearance, powerful expiratory efforts made their appearance accompanied by loud phonation, and on cessation of respiration no sign of heart beat could be found.

P.M. Chest opened rapidly. Ventricles fibrillating, auricles beating, right auricle purple, left auricle bright red



*(b) Observations made with recording apparatus.*

I have succeeded in obtaining graphic records of nearly all the forms of sudden syncope which have just been described as occurring during the induction and recovery stages, and as will be seen, they all conform to the same type, *i.e.*, a sudden collapse of the circulation, invariably preceded by a typical irregular tachycardia.

I have made many and persevering attempts to obtain graphic records of these forms of sudden death occurring in the course of the process of the induction of anæsthesia, but, with some important exceptions, the experiments did not prove very fruitful of results. Even in intact animals there is no exact procedure which will *insure* the onset of syncope at this stage; a number of trial experiments must be performed before attaining a single positive result. At times a succession of successful reactions have been obtained, but I have never been able to fathom the particular circumstances attending the success of the experiments, and that in spite of modifying the general conditions of the animals in regard to feeding, &c., in many ways; a distinct impression is left that the tendency to ventricular fibrillation is one of seasonal incidence. Under experimental conditions with vascular and respiratory recording apparatus the difficulties of this form of research are multiplied. In one series of experiments I adopted the method of Brooks, by this means following the process of induction from the very commencement, but under these conditions the heart appears to be somewhat less liable to pass into an irregular condition than usual. The preceding operation no doubt tends to depress the heart and exhaust the suprarenals, for the results are different in degree from those observed in normal intact, and hence vigorous, animals.

A second series of animals was submitted to a preliminary anæsthetisation by pithing the cerebral hemisphere; but this method has likewise proved unsatisfactory, for the heart appears to be depressed under such circumstances and, as has already been remarked, the ventricles fail to fibrillate even when directly stimulated by the injection of adrenalin.

*The effect of struggling.* In one experiment with Brooks' method I obtained a very significant tracing. As a general rule in this method the stage of muscular excitement, which is so frequently observed in normal cats, is suppressed, but in this single animal I did manage to induce an excitement stage accompanied by struggling. The heart thenceforth assumed an irregular tachycardial condition which very quickly passed into fibrillation of the ventricles, and a precipitate fall of blood-pressure from a height of 180 mm. took place. This experiment is illustrated and fully described in Fig. 19. There was no excessive intake of chloroform in this experiment, even if such be a possible event at 1% concentration; further, the chloroform was stopped before death, and this fact may have even accelerated the syncope. The large fluctuations seen in the respiratory curve are not wholly due to deep breathing, but in part to a mechanical disturbance of the recording



bag through muscular movements, and in fact the animal must have been holding its breath to a certain extent whilst struggling, for the colour of the left auricle was darker than is usual in death from ventricular fibrillation.

With the exception of the exposed artery this animal was otherwise intact, and the experiment may be taken as typical of what happens in death from struggling in the early stages of anæsthesia, which is thus proved to conform to the usual type of death from ventricular fibrillation under light anæsthesia illustrated in previous sections of this paper. I have on many occasions likewise observed struggling cause an already irregular heart to fibrillate in the course of the later stages of an experiment, but these were generally fortuitous occurrences and were unrecorded. Struggling is most deadly after entire removal of the chloroform or after it has been reduced to a very low percentage.

As regards the mode of action of struggling I think there can be little doubt. For some time the relation of a rise of blood-pressure (the mechanical effect of powerful movement) interested me, but although in unanæsthetised animals movement gives rise to considerable alterations in blood-pressure, in the chloroformed animal this effect is largely negligible. I think it can hardly be doubted that the onset of irregularities is the outcome of a state of general excitement, affecting the sympathetic as well as the somatic nerve paths. The subjective evidence of cardiac acceleration in emotional states is a commonplace observance; apart from this it has been shown by Cannon and de la Paz,<sup>3</sup> and later confirmed by Elliott,<sup>4</sup> that emotional states, such as fright or anger, are accompanied by an increased secretion of adrenalin. In this way in all probability the usual double effect, accelerator and suprarenal, is brought to bear on the heart—just as it is in the case of ventricular fibrillation following a sensory stimulation. Ventricular fibrillation may also be produced under chloroform through the action of strychnine, or by pithing the spinal cord, and in fact I conclude that any convulsive nervous output, such as that which may be said to accompany struggling, may result in a cardiac syncope from ventricular fibrillation.

It is thus seen how the excitement phase of the induction period is a very dangerous one. Violent movements are liable to be accompanied by the onset of cardiac irregularities which may quickly pass into fibrillation or may constitute the precursors of fibrillation from other causes. The onset of these irregularities from struggling may be confirmed with the utmost readiness in the intact animal by such simple means as placing a finger over the apex beat, or by the use of a stethoscope.

*The effect of removing or decreasing the chloroform.* In Fig. 20 is shown the result of taking off the chloroform, in this case of 1% concentration, in the course of the earlier stages of anæsthesia. There is a prompt increase in the efficiency of the heart's action, resulting in a rise of pressure, and a subsequent transition into an irregular tachycardia of brief duration. I have had many opportunities of observing a similar



reaction at later stages of anæsthetisation ; the heart does not then react so promptly, but I have observed on several occasions ventricular fibrillation to occur as a purely spontaneous sequence to a ventricular tachycardia induced in this manner.

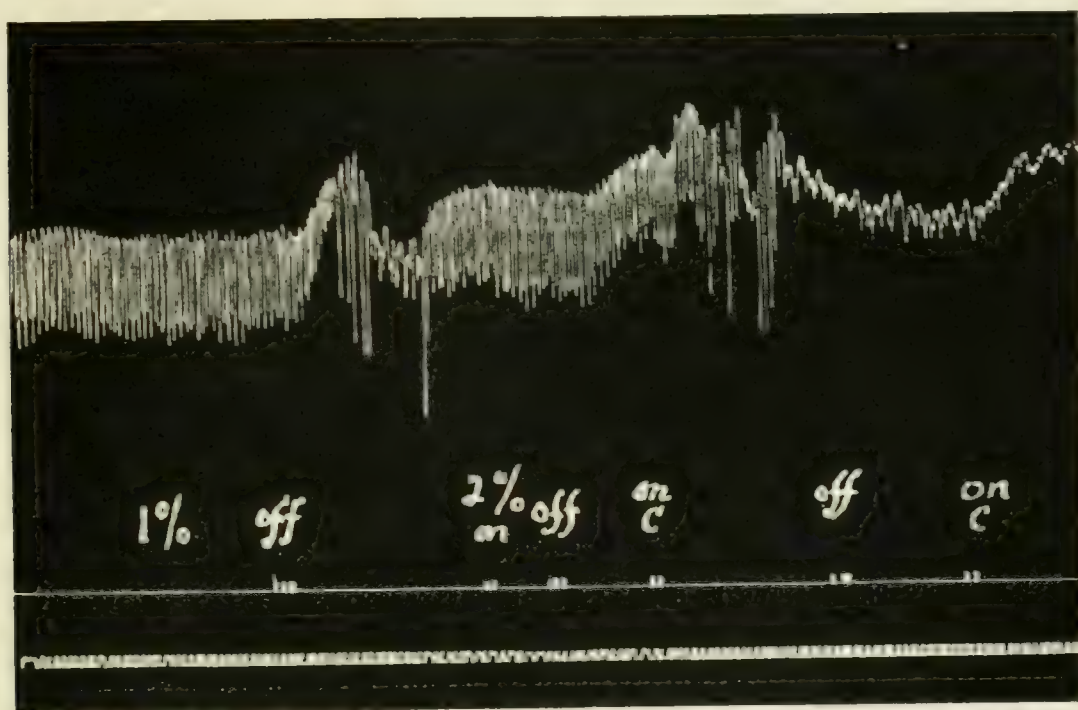


Fig. 20. Blood-pressure curve during the later stages of the induction of anaesthesia (Brooks' method). Cannula in crural artery.

The heart is stimulated by taking off 1% vapour and passes into a phase of irregularity. The heart fails to respond on re-applying a 2% vapour. On taking off 2% the heart responds once more by a rise of blood-pressure. A glass tumbler containing a piece of wool saturated with chloroform was then put over the animal's head ("on C"), causing the onset of an irregular tachycardia. A later re-application of concentrated chloroform is seen to cause a rise of blood-pressure. The signal line represents the 50 mm. pressure level. Ludwig manometer. Time in seconds.

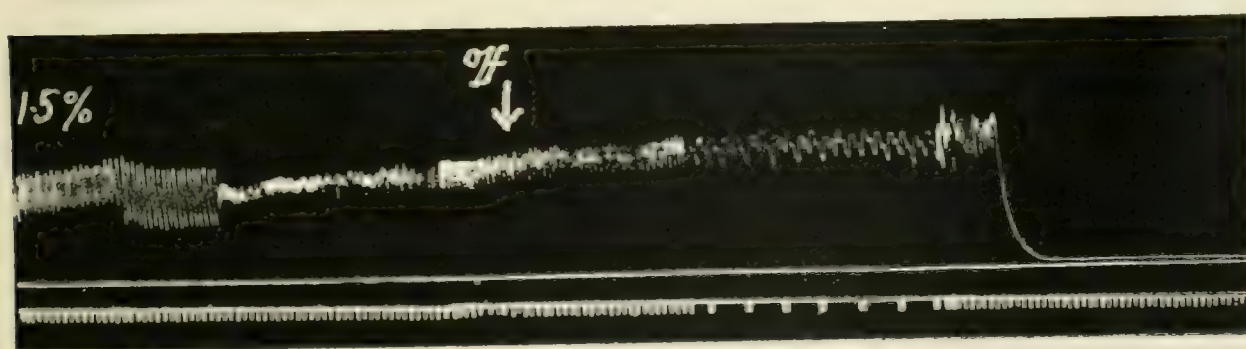


Fig. 21. Ventricular fibrillation resulting from partial recovery from chloroform anaesthesia. At the beginning of the tracing the kymograph was stationary, 2.2% being administered ; the chloroform was reduced to 1.5% and the drum started. The arrow marks the moment of entirely removing the chloroform. At one point the drum is accelerated to demonstrate the cardiac irregularities. For further details see text. Hürtle manometer. Time in seconds. Just before the arrow mark the tracing is slightly blurred owing to a fault in the tracing paper.

Fig. 21 illustrates one out of several tracings I have obtained of this event.

This cat had been under a 2.2% vapour at the commencement of the tracing. The result of reducing the vapour to 1.5% was an increase in

cardiac action and a rise of pressure from 72 to 88 mm., the rate of beat being 120 per minute. This rhythm suddenly changed to a bigeminal beat, and this again passed into an irregular tachycardia. Forty seconds later the chloroform was removed entirely; the blood-pressure continued to rise, and after a period of intense tachycardia (about 360 beats per minute) the ventricles fibrillated. This occurred about 45 seconds after removing the chloroform, the ultimate height of blood-pressure being 102 mm.. The animal was perfectly quiescent throughout the experiment, and at its termination it could not be said to have more than partially recovered, as is evidenced by the comparatively low level of the blood-pressure just before fibrillation occurred.

In this and in several similar tracings I have obtained a complete graphic representation of such events as have been described in previous pages as the result of taking off the chloroform, and the process is demonstrated to be exactly similar to that resulting from the action of adrenalin or that of sensory stimulation in that an initial stage of cardiac irregularities precedes the fibrillation.

In Fig. 8 the effect of taking off the chloroform has been illustrated under other circumstances; the irregular tachycardia was initiated by an irritation of a sensory nerve, but this alone would not have served to throw the ventricles into fibrillation under the existing concentration of chloroform, viz., 1.5%, it was only on taking the chloroform away altogether that this came about. In this way irregularities initiated by struggling, or in other ways during the induction period may terminate in ventricular fibrillation if the administration be subsequently intermitted.

Similarly I have seen on one occasion ventricular fibrillation occur on ceasing the administration of a high percentage of vapour on account of signs of an impending overdose, the breathing having become nearly, but not quite, suppressed. The blood-pressure then rose rapidly, the heart became irregular, and the ventricles fibrillated at a blood-pressure of 122 mm.. It is easy to understand how, but for the fortunate accident of a tracing, such a fatal result might have been attributed to cardiac depression alone from excessive chloroform.

It is an open question whether in the earlier stages of anæsthetisation another factor may not assist in bringing about a fatal result: this is the stimulation of the nasal mucous membranes by a change from chloroform vapour to pure air. This is not a mere fanciful suggestion, for undoubtedly this change of atmosphere does stimulate the nasal mucosa, as is evidenced by the severe fits of sneezing which frequently follow immediately upon removal of the chloroform. The onset of fibrillation is sometimes so rapid that it does seem at least *possible* that a reflex factor such as this may be involved.

The onset of spontaneous irregularities on a transition to a lighter degree of anæsthesia is a conspicuous event at all stages in the course of experiments under chloroform. If the transition be a gradual one, as may be



the case when the heart has been under the influence of chloroform for some time, the irregularities may appear in a graded sequence from single extrasystoles up to the more complicated tachycardias, a sequence which is in conformity with the view that these different forms of irregularities are expressions of progressive grades of the same pathological process (*vide* Levy and Lewis<sup>21</sup>). In Fig. 22 is illustrated such a slow transition arising from the substitution of a 0.5% vapour for a 2.7% vapour. As the animal passes into a lighter degree of anæsthesia the blood-pressure rises and the heart accelerates slightly so long as it remains regular, starting at a rate of 144 beats per minute and finishing at a rate of 156 per minute just previous to the onset of the first extrasystole, the blood-pressure having in the meantime risen from 88 mm. to 118 mm.. Following this the heart again becomes regular for a few seconds and then breaks into a sequence of trigeminal beats, followed by a series of mixed bigeminal and trigeminal beats. Finally a rapid indecipherable tachycardia ensues, broken at irregular intervals by long pauses.\*

The most intense irregularities in such cases appear in the lighter degrees of anæsthesia, the intermediate forms in the intermediate degrees of anæsthesia. It is not my view, however, that chloroform in a particular degree of concentration can of itself initiate a specific form of irregularity, but the onset of irregularities is, I believe, conditioned by the *change of cardiac state* involved in the progress from deep to light anæsthesia; as the change progresses the irregularities become more marked. Chloroform serves to render the ventricles *irritable*, *i.e.*, liable to exhibit beats of heterogenetic and ectopic origin, but these only occur when it is subjected to some further form of *exciting* cause, such as a cardiac stimulation. The heart may be maintained beating at a perfectly regular rate even when lightly anæsthetised so long as the anæsthesia is a level and unchanging one, and no other disturbing influence is at work, such as arise from sensory stimulations. This is best seen in the intact animal. If a cat be anæsthetised gradually with chloroform and kept quiet and undisturbed the whole time, the heart continues to beat regularly even when the anæsthesia is light. Thus in one instance a cat was anæsthetised with a 1% vapour, it was petted and stroked, and remained perfectly quiescent until it became unconscious. The same vapour was administered continuously for thirty minutes, and the heart remained perfectly regular the whole time.† If, however, in a cat so anæsthetised, the chloroform be entirely removed, the heart is liable to become irregular, and the ventricles may eventually fibrillate. Similarly, irregularities may appear, not on total withdrawal, but on a change to a lighter degree of anæsthesia alone, and I have little doubt that the exciting cause of the ectopic beats is identified in the change of cardiac state involved in its release from the

---

\* Indicated by the drops in the curve.

† A like result was obtained on administering 0.7% chloroform for over an hour. A few extrasystoles were in this case noted during a short period of violent retching.

depressing action of the chloroform, this release being, in effect, the equivalent of a cardiac stimulation, just as release from the depression of vagal control is the equivalent of a cardiac stimulation.

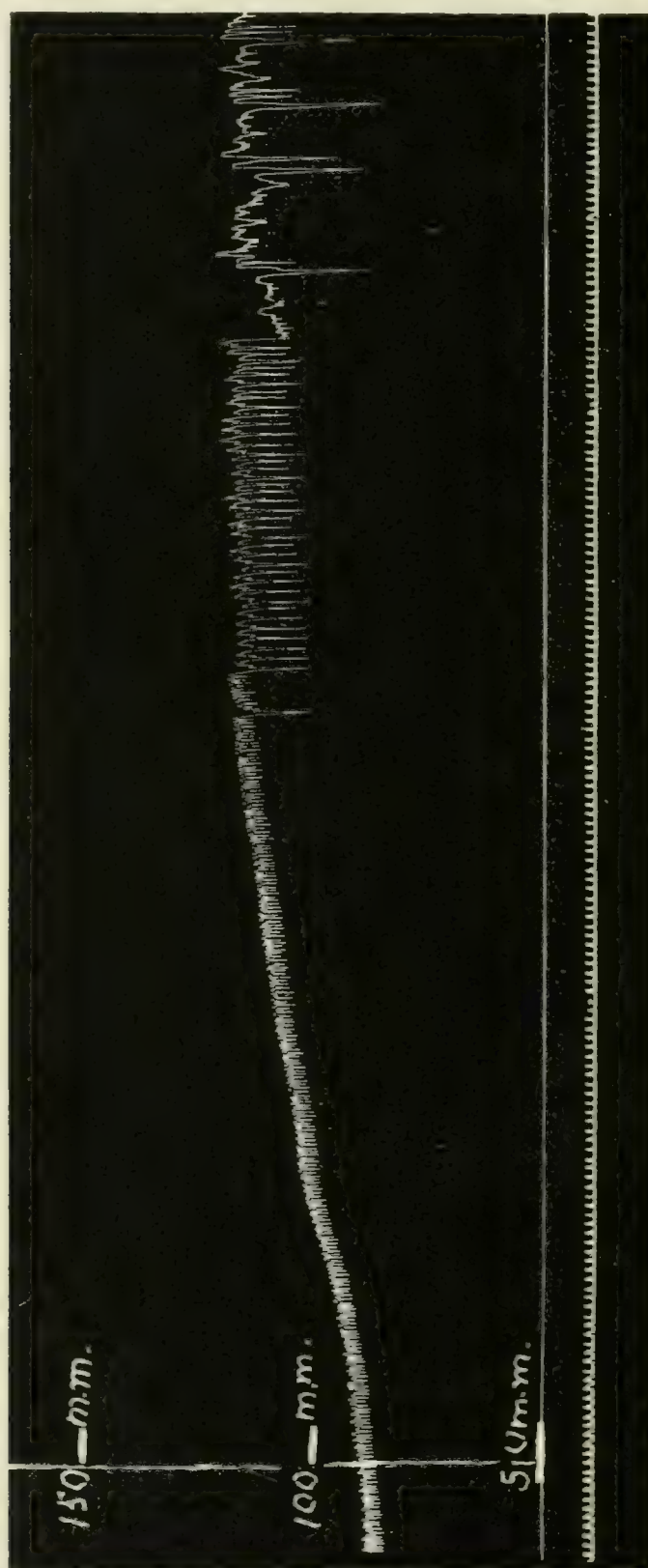


Fig. 22. A rise of blood pressure followed by progressive stages of irregularities resulting from the passage from a deep to a light anaesthesia; for detailed description see text. Ludwig manometer. Vertical scale indicates blood pressure. Time in seconds.

The depression of cardiac function by chloroform is an accepted fact, and I need give but a single reference in this connection, viz., the work of Sherrington and Sowton<sup>26</sup> upon the isolated mammalian heart. These



experiments demonstrate a progressive depression of the force of ventricular contraction down to extinction on perfusion with solutions of chloroform of progressive strengths, the rate of heart beat remaining unaltered ; on washing out the chloroform from the heart this regains its full force of action once more.

In the intact animal a similar effect is noted ; on removing the chloroform the blood-pressure rises, mainly through the increased efficiency of the heart beat ; there is also, however, in this case, distinct evidence of acceleration on recovery, but this is never, so far as I have observed, a very marked acceleration, comparable, for instance, with that resulting from section of the vagi (I am speaking, of course, of rhythmic acceleration only, and not accelerations due to heterogenetic beats). In the instance already cited (Fig. 22) the acceleration was 144-156 with a pressure rise of 30 mm. ; in another instance the change of rate was 127-150 with a pressure rise of 35 mm. ; in yet another case the change of rate was 108-144 with a pressure rise of 26 mm.. It must be admitted therefore that this form of stimulation is possibly somewhat different from that occurring on section of the vagi, and it appears probable that the stimulation arising from recovery of depression caused by chloroform affects the heart mainly in respect of one of its functions, viz., its force of action. This particular function is predominantly affected by the action of adrenalin, it is affected equally with acceleration as a result of nervous stimulation or of vagal section, and it is thus uniformly affected in all my experiments ; it is, however, impossible to allocate at present to any one function of the heart a chief part in the mechanism of the production of ventricular irregularities ; all the functions so far as is yet known may play a part.

These considerations afford an indication of the manner in which high percentages of chloroform vapour serve as a protection from the incidence of ectopic beats and ventricular fibrillation. Apart from its depression of the reflex nerve centres, deep narcosis tends to depress and dilate the ventricles, and thus by a direct cardiac action counteracts the effects of stimulation, either totally, so that the heart remains regular, or in part, so that although abnormal beats may be excited, yet the stimulation cannot produce its most profound effect, viz., ventricular fibrillation.

Interesting support to the above observations and considerations is afforded in some casual observations by Sherrington and Sowton<sup>26</sup> in their experiments already referred to. In a table of results (British Medical Journal, July the 23rd, 1904, p. 168), it is noted that on washing out a strong chloroform solution from the perfused heart and thus allowing it to recover, it was liable to pass through a stage of fibrillar contractions. I gather that this was observed in the *recovery* stage only, and never during continuous administration with any concentrations of chloroform in the perfusion fluid. These observations are likewise interesting as tending to confirm my suggestion that the ventricular fibrillation arising from stimulation of the heart under chloroform is an intracardiac and not a nervous phenomenon.

*The re-application of chloroform.* It has been seen how reduction of the anæsthetic may initiate cardiac irregularities, which may terminate spontaneously in fibrillation, or may terminate in fibrillation as a result of the added stimulus of struggling or of re-application of the vapour. This latter procedure has now to be considered. When first noted, I was unable to decide whether death was a *post hoc* or *propter hoc* effect of re-application, but the great frequency with which the two events have been associated leaves no room for doubt that the one is the exciting cause of the other.

I have already cited several cases of death from this cause which prove that it may be brought about by chloroform vapour of ordinary anæsthetic strength, *i.e.*, at or under 2%, but it does appear to be more readily conditioned by a vapour of higher concentration, and by using such stronger vapours graphic records have been obtained on several occasions. In Fig. 20 the effect of re-application in the earlier stages of administration is shown; 2% is ineffective, but a concentrated vapour causes the heart to pass into an irregular tachycardia. I have on several occasions been enabled to obtain tracings showing ventricular fibrillation as a result of re-applying a concentrated

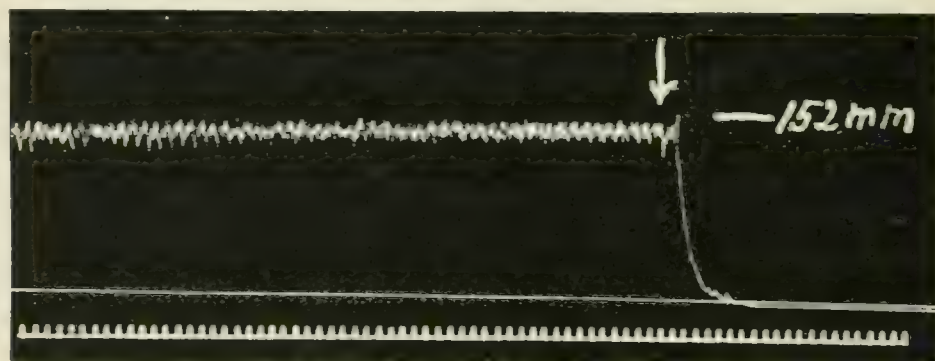


Fig. 23. Ventricular fibrillation resulting from the sudden administration of a concentrated vapour to a cat which had not been inhaling any chloroform for two minutes, the heart exhibiting a rapid irregular tachycardia. The animal was perfectly quiescent but the application caused a slight general reflex spasm, and was almost immediately followed by V.F. The arrow marks the moment of re-application. Hürtle manometer. Time in seconds.

vapour to an animal not under any anæsthetic at the moment, and in which the heart was already in a state of tachycardia; Fig. 23 shows this reaction very well. In this case the reaction was almost instantaneous, as it generally is, but it may be delayed as much as 30 seconds from the moment of re-application. It is conclusively shown in this tracing that the cardiac syncope was not the result of an "overdose" in the ordinary sense of the word, although the vapour was certainly very strong, being exhibited by putting absorbent wool containing a considerable quantity of chloroform into a glass tumbler, and putting this over the head of the cat. There was, however, not sufficient time before syncope occurred, for the vapour to produce any depressing effect, as is evidenced by the fact that the blood-pressure at its final elevation was 152 mm.. The cat was, in fact, still lightly anæsthetised when it died.



When a strong irritating vapour is given suddenly to a lightly anæsthetised cat it may, and often does, cause the animal to struggle, and this struggling alone may then of course account for fibrillation. When struggling does not occur, a slight general muscular twitch is frequently observed at the moment of re-application; the animal appears to become slightly tense, as was the case in the experiment from which Fig. 23 was taken, and this fact points to the probability that the onset of fibrillation is conditioned largely by a reflex sensory stimulation, just as an irritant vapour like ammonia produces a reflex cardiac effect.

Apart from the above considerations it appears probable that the first effect of chloroform upon the heart is a stimulating one, and there is in fact direct evidence of this in the experiments of Sherrington and Sowton<sup>26</sup> already alluded to; the effect is not a very marked one, but it is perfectly evident and is remarked upon by the authors. In this respect chloroform shares with most other anæsthetics the property of being a stimulant in the initial stages of its action.

It is, therefore, highly probable that the effect of re-subjecting the heart to chloroform, after having allowed the former effects of the anæsthetic to partially wear off, is a further stimulation of the ventricles through both reflex and direct means, and in this way constitutes a further exciting cause of ventricular fibrillation.

The fact that the re-application effect is more readily observed when the vapour is strong constitutes, so far as I have observed, the only particular instance in which a strong vapour more readily conduces to ventricular fibrillation than a weak one, and this greater facility of causing syncope with a stronger vapour in this single set of circumstances has, I believe, been mainly responsible for the support which has been accorded to the idea that all deaths under chloroform are the result of overdosage. To this point I shall refer again later.

(c) *The apparently spontaneous deaths in man during the induction and recovery periods of chloroform anæsthesia.*

I have dealt at considerable length with the induction stage of chloroform anæsthesia in animals, because it is one of great practical importance, for a majority of the deaths in the chloroformed human subject occur before the operation has been commenced. It is stated (*vide* Leonard Hill, British Medical Journal, April the 17th, 1897) "that in one year, out of forty-one recorded deaths from chloroform, thirty-nine occurred during the primary stage of anæsthetisation and before the surgeon had touched the patient." In John Snow's book fifty fatalities are recorded, and out of these twenty-eight occurred before the operation was started.

In an appendix to the Report of the Anæsthetic Committee of the British Medical Association (July, 1900) there is a collection of chloroform fatalities which appeared in the press in the year 1892. These deaths number twenty-four, and of them, fourteen occurred during the period of induction of

anæsthesia, and four (Nos. 4, 7, 15 and 18) after completion of the operation and while the patient was recovering. Out of these fourteen induction cases seven were too briefly reported to allow of any analysis (Nos. 1, 9, 10, 11, 17, 20 and 22). In one case (No. 2) death was obviously due to *intermission* as the chloroform container of the Junker inhaler became detached, a fact which was discovered after death. In one case (No. 13) *struggling* followed by *intermission* was the cause of death. In three cases (Nos. 5, 18 and 12) *struggling* alone killed the patient. In one case (No. 23) *struggling* and *re-application*, and in the other (No. 16) a fit, described as epileptic,\* immediately preceded death. The remaining cases are referred to later in this paper.

I give here a single instance of a completely reported case taken from Snow's book on Anæsthetics; it serves as an excellent clinical counterpart to some of the cases of death during induction in cats related in this paper, all the three causal factors of syncope, viz., excitement and struggling, intermission and re-application being particularly well defined. There can be no question but that this man died from ventricular fibrillation.

*CASE 17.* "The patient, a man, thirty years of age, was affected with hydrocœle. The chloroform was poured on a little cotton, which was placed at the small end of a cone, into which the folded towel made use of was rolled. About a drachm and a half was first poured on the cotton, and the patient was told to inhale in long and deep inspirations. This quantity being nearly evaporated in two or three minutes, a drachm more was added. After a few inspirations rigidity and struggling came on; these subsided, but in a little time returned more strongly than before, and the towel was removed from the face until the struggling ceased. The patient, however, not being sufficiently insensible to undergo the operation with the necessary quietness, the towel was re-applied, when, after a few inspirations, the pulse suddenly ceased. The face and the whole surface of the body turned pale, the eyes rolled upwards and inwards, and the breathing became very slow, but full and deep, the intervals between the inspirations becoming longer, until the respiration ceased altogether. The patient died before the operation was begun, and within five minutes from the commencement of inhalation. During the application of various means of resuscitation, including the dropping of cold water *guttatim* on the epigastrium, the breathing returned and continued for the space of three or four minutes; but the pulse and sounds of the heart did not return."

The exact procedure adopted during induction is rarely recorded in reports of chloroform syncope. The method is generally an intermittent one, and is frequently characterised by a *want* of method. The patient may be inhaling chloroform one minute and inhaling none the next, so that the administrator may be unaware of the extent of the intake of vapour, much less be able to report it. I have, however, selected three other cases of death during the induction period for insertion in the Appendix to this paper (Nos. 3, 4 and 5) as they present points of some interest; in one of them the percentage of vapour inhaled is recorded.

In those cases in which the patient dies during recovery from anæsthesia on completion of an operation, the anæsthetist's attention is usually relaxed, and precise details are in consequence lacking. The following is a typical report of this kind:

*Lancet, September the 11th, 1897.* "A boy, aged fifteen years, had been anæsthetised with chloroform for the removal of post-nasal adenoids. The operation had been completed and the anæsthetic withdrawn, when the patient was noticed to be breathing deeply. The operator observed some peculiarity about the colour of the face, but was reassured by the presence of free respiration. The respirations, however, suddenly ceased, and all efforts to resuscitate the patient failed."

---

\* A so-called epileptic fit is not infrequently alluded to in reports of chloroform fatalities. It probably corresponds to the terminal asphyxial convulsions noted in my experiments.



## DISCUSSION.

The facts given in this paper throw an entirely new light upon the cause of death under chloroform, and provide data competent to explain every form of death under chloroform which has been described in the human subject. A few typical cases have been described in this paper, but a full clinical discussion of these new facts must be reserved for a paper dealing more particularly with this aspect of the matter.

The large mortality incidence of the induction period in the human subject is fully explained on the basis of my theory of death under chloroform; the induction stage is *par excellence* the stage of light anæsthesia; it is moreover the stage of excitement. Very little chloroform has been packed away in the tissues of the body in the earliest stages of administration, and this little is excreted with remarkable rapidity on lessening the alveolar vapour tension of chloroform, and hence the patient "comes round" with great readiness; this is a fundamental clinical experience. It is remarkable that the prevalence of death in the induction period has never before been associated with this period, regarded as one of *light anæsthesia*.

In the series of twenty-four cases referred to, published in the Appendix to the Anæsthetic Committee's Report, eighteen have already been mentioned as occurring during the induction and recovery stages. In the remaining six the operation had been commenced. One of these (No. 19) was an unexplained case of "respiratory failure" occurring after the patient was put back to bed. In two (Nos. 14 and 26) the death was caused by *re-application* after an interval during which no anæsthetic was given, in the early stages of operation. In one case (No. 24) death occurred *on the first incision*, and in the remaining case (No. 25) the patient died in the early stages of operation, having shown abundant evidences of imperfect anæsthesia.

It is a remarkable fact that in not one of these cases was there any suggestion that an overdose of chloroform had been given, or in fact any evidence to support such a view. This indeed is the common story—the evidences of light anæsthesia entirely outweigh those of deep in nearly every case in which sufficient clinical details are given to enable one to form an opinion.

It is not surprising that the Anæsthetics Committee arrived at certain sweeping conclusions regarding the dangers of incomplete anæsthesia (see pages 122 and 123 in their Report). These conclusions were based on an elaborate analysis of a large number of reports of cases, mainly cases of the administration of chloroform and its mixtures, and they constitute the strongest possible support to my views regarding the source of danger under chloroform; it is in fact almost incomprehensible that the bearing of this valuable report should not have been better appreciated. This danger of light anæsthesia as opposed to deep is, it is pointed out, associated with the administration of chloroform, and not of ether.

The following important conclusions in regard to chloroform are stated among the final general conclusions in this report :

“XVI. When danger occurs under chloroform, whatever its exact nature may be, there is abundant evidence that in a large proportion of cases the symptoms that are observed are those of primary circulatory failure.”

“XVII. Imperfect anæsthesia is the cause of a large number of cases of danger under chloroform.”

“XIX. Struggling is very much more frequent in the complicated cases under chloroform than in the uncomplicated, and this phenomenon must therefore be regarded as a source of grave danger under chloroform.”

In the face of these findings, it is somewhat surprising to find that the accepted theory of death under chloroform remains that of overdosage, and the accepted theory of safe administration is the limitation of the strength of vapour to the very lowest point of efficiency.

It is impossible within the scope of this paper to deal with the immense amount of controversial literature upon the subject of chloroform syncope, or to follow the work which has led to the adoption of this theory, but the main features are as follows :—

One of the earliest and most scientific workers on chloroform, John Snow,<sup>27</sup> expresses himself as follows (pp. 120-121) :—

“If it were possible for a medical man to mistake or disregard the symptoms of approaching danger, and to go on exhibiting vapour of chloroform, diluted to a proper strength, till the death of the patient, this event would take place slowly and gradually, as in Experiment 23, related above, and every other experiment in which the air did not contain more than five per cent. of vapour. The action of the heart would survive the respiration ; there would be a great tendency to spontaneous recovery, and the patient would be easily restored by artificial respiration, if it were performed whilst the heart was still acting ; *as I have always found it to be successful in animals under these circumstances.*”

The truth of these words is practically admitted by all subsequent observers ; Paul Bert,<sup>1</sup> working with vapours up to 5.4% strength, concluded likewise that the heart always continued to beat after the cessation of the respiration as a result of overdosage. I may add on my own authority<sup>19</sup> that chloroform, when administered to the human subject by ordinary methods, cannot exceed 6% in concentration and can rarely approach that value. There is no evidence to show that higher percentages than 6%, when *continuously* administered till overdosage ensues, will affect the heart in any other fashion, or that recovery is any the less possible when promptly attempted. Observations on the *continuous* administration of vapours of higher than 6% value are wanting so far as I am aware ; but there is no reason to believe that the heart is in such cases affected in any different manner : such observations would be in any case of little practical importance, for these percentages are outside the range of ordinary usage.

How then does the theory of sudden death from overdosage come about ? Snow was well aware that all *fatal* cases of chloroform syncope were due to primary cardiac failure, and the Anæsthetics Committee so recently as 1900 came to a very similar conclusion. Unfortunately Snow was the servant



of his method, viz. : the titration of doses, and he appears to have sacrificed his better judgment in the interests of this method. He apparently searched about until he found a procedure which appeared to prove that very strong vapour, i.e., 8% to 10%, would produce the primary cardiac failure he was looking for. The fallacy underlying Snow's conclusions will be apparent from the following quotations from his book :—

Page 116. "In every instance in which the quantity of vapour in the air breathed by the animals was from three to six per cent., the respiration ceased whilst the sounds of the heart were still very distinct ; in many instances the heart continued to beat from two to three minutes after the breathing had ceased. . . . . When, on the other hand, the air breathed by the animals contained eight or ten per cent., or upwards, of vapour or chloroform, the action of the heart was always seriously affected and rendered extremely feeble, if it did not actually cease, at the time the breathing was arrested. In several instances, indeed, the sounds of the heart entirely ceased before the breathing, as in Experiment 25, and although the chloroform was withdrawn . . . . it very rarely had the effect of restoring the heart's action."

The experiment No. 25 referred to above, and upon which Snow relies as one of his chief arguments in favour of the occurrence of sudden and permanent heart failure as the result of overdosage, may be briefly abstracted as follows :—

Page 111. "A cat was placed in a jar containing 4% chloroform vapour. It was removed in a passive state at the end of two and a half minutes. The respirations and heart sounds were quite natural. It was then made to breathe through an inhaler yielding a strong vapour (presumed to be about 10%). After four or five inspirations from the inhaler the heart ceased to beat, the respirations still going on. The inhaler was removed when the heart ceased to beat, and there were two or three rather convulsive respirations afterwards, and then the breathing stopped. The chest was opened ten minutes after death. The heart appeared quite motionless when first observed, but after exposure to air for a short time, there were some slight contractions of a few fibres of the right ventricle."

Overdosage had no direct relation to the fatal result of this experiment, for the procedure was that of *intermission* and *re-application* which I have repeatedly demonstrated to result in fatal syncope with *vapours of ordinary anæsthetic concentration*. It is, for instance, strictly comparable with case No. 14 on page 357 in which the strength of vapour never exceeded 2%.

In the whole of the experiments upon which Snow founded his theory of primary cardiac syncope from the inhalation of strong chloroform vapour (those which he has published are but few in number) similar confusing factors are palpable, that is to say, interrupted administration, struggling and re-application of vapour. In fact there would not appear to be anything in these experiments that cannot be produced by an ordinary anæsthetic strength of vapour. (*Vide* p. 119 in Snow's book.)

Snow's comments upon the fifty collected cases of chloroform fatality are a revelation in perverted interpretation. In many the evidence of primary cardiac syncope, which he acknowledges, is graphically described, but at the same time the evidences of light anæsthesia are remarkably clear ; yet Snow persistently ascribed these deaths to the action of an excessive vapour of over 8%. In some of these cases Snow's own inhaler was employed, which he estimated did not supply more than a 4% vapour,\* but this fact did not suffice to satisfy him of his error.

---

\* Normally this apparatus does not yield more than 3.5% vapour with a medium force of inspiration.

Unfortunately chloroform research has followed on much the same lines ever since ; no doubt the fact that a strong vapour is more effective than a weak one in producing the "re-application" effect has conduced to the survival of this error. MacWilliam<sup>22</sup> fell into exactly the same pitfall. He observed sudden cardiac failure in three instances in cats, and on the evidence of these instances alone he appears to have satisfied himself that primary cardiac syncope may occur as a result of overdosage. These three cases are fully described ; they belong most distinctly to the category of death from intermission and re-application, and are undoubtedly the result of ventricular fibrillation.

There is, with the exception of Embley's work, no other experimental evidence upon which a theory may be formulated of death from primary cardiac syncope under chloroform as a result of overdosage.

Dr. Embley's<sup>5</sup> work on the vagal phenomena of the induction period is too well known to require much comment, but his results are of somewhat doubtful practical significance. The liability of the heart to vagal inhibition was demonstrated in animals which had been very heavily dosed with morphia in addition to chloroform, 0.25 to 0.5 grammes of morphia, and the tendency of morphia to favour vagus effects is well known.

Embley likewise reproduces two tracings which demonstrate, in non-morphinised animals, a similar cardiac inhibition occurring at a blood-pressure level of 25 mm. Hg. or thereabouts, as a terminal event following the administration of concentrated, unmeasured, doses of chloroform, sufficient to depress the heart rapidly. Such experiments have no clinical counterpart, and further there can, I think, be no question at all, on the evidence of Embley's own tracings, that the heart so inhibited is subject to recovery in every case on the prompt application of restorative measures. Embley's experiments never favoured the chances of recovery, although the tendency to recovery was obvious, and it still remains to be shown that this vagal effect of overdosage may be in fact a cause of irrecoverable, *i.e.*, fatal inhibition of the heart.

There remains the prevalent idea that sudden death may result from the *reflex* inhibition of the heart through the vagi, although this of course has no relation to overdosage. This theory I have already discussed at some length on page 347, and I have shown that there is no valid evidence to support it.

I may here briefly refer to two observers who have worked on less conventional lines and have been nearer to arriving at a true conclusion.

The late Dr. Robert Kirk<sup>12</sup>, who held strong opinions regarding the relation of light chloroform anæsthesia to sudden death, performed an extensive series of experiments in which he observed, by means of a stethoscope, intense cardiac irregularities resulting from a suspension of the administration of chloroform, and in one case he noted the entire cessation of cardiac action



for 60 seconds ; I have derived some valuable indications from his papers. Dr. Kirk refers to MacWilliam's work on ventricular fibrillation and suggests it as a possible explanation of the question. Professor Fraser Harris has kindly sent me some unpublished tracings of experiments performed by him in conjunction with Dr. Kirk in which various irregular tachycardias occurring under light chloroform anæsthesia in a cat may be recognised. Another tracing shows a period of complete heart failure in a dog poisoned with phosphorus and under chloroform. Unfortunately Dr. Kirk did not follow up this line of research further, but formulated a theory which did not find general acceptance.

The other observer is Dr. Alex. Wilson<sup>30</sup> who was led to believe from clinical observations alone that human subjects died from sudden vascular failure under light anæsthesia. From the observation of the occurrence of convulsions and asphyxial respiratory spasm (such as he had seen on the rupture of an aneurysm and in like cases) he deduced a sudden collapse of the circulation, an acute application of physiological principles, but his further suggestion that the event was due to a sudden vasomotor paralysis has not received confirmation.

MacWilliam<sup>22</sup> observed ventricular fibrillation on several occasions in chloroformed animals. He thought that it was conditioned by an excess of vapour. It is natural that he failed to find it, in this connection, a satisfactory explanation of sudden death. He concluded that "it does not appear to be a primary mode of cardiac failure from the inhalation of chloroform in the healthy animal."

This brief review of the work performed upon chloroform syncope tends to show that there is no mechanism with the exception of ventricular fibrillation which can be demonstrated to bring about a rapid and permanent primary cardiac syncope. This is a condition peculiar to light and not to fully established chloroform anæsthesia.

I may add a final word to explain my views in regard to overdosage. Of course animals and men can be killed by the persistent administration of chloroform, and the stronger the vapour the more rapid the death. This has been abundantly demonstrated in animals. It has also been abundantly demonstrated that overdosed animals recover if the ordinary means of resuscitation are promptly applied. So in man ; the respiration, and even more rarely the radial pulse, may be suppressed by overdosage, yet recovery is brought about by prompt measures of resuscitation, generally very readily so ; it is inconceivable that such measures should be too long delayed even in the hands of the most casual administrator of anæsthetics. I will concede that repeated overdosage may prove fatal, or that overdosage in an asthenic individual may prove fatal, but I do not believe fatal overdosage ever occurs as a result of ordinary anæsthetic methods in those sthenic individuals who form by far the greater proportion of the victims of chloroform anæsthesia.

## GENERAL CONCLUSIONS.

1. The mammalian heart, when under the influence of chloroform, is in an "irritable"\* condition. This irritability is raised under conditions of light anæsthesia, and lowered under conditions of deep anæsthesia.

2. Abnormal ventricular beats are evoked in a heart under chloroform by conditions which stimulate it or by equivalent conditions which remove or reduce depressing influences.

3. Under conditions of light chloroform anæsthesia the ventricular irregularities resulting from cardiac stimulation may terminate in ventricular fibrillation and death of the heart.

4. Stimulation of the heart may be effected :—

- (a) As a reflex from sensory excitation ;
- (b) As a result of an intermittent administration of the anæsthetic.
- (c) As a result of the state of nervous excitement accompanied by struggling induced by chloroform in the earlier stages of its administration.

5. Ventricular fibrillation is a cause of death under chloroform, probably the only cause of any moment. It can be prevented by steadily maintaining a full degree of anæsthesia.

## BIBLIOGRAPHY.

- <sup>1</sup> BERT. *Compt. Rend. de Soc. Biol.*, 1883, v, 241.
- <sup>2</sup> BROOKS. *Heart*, 1910, II, 5.
- <sup>3</sup> CANNON AND DE LA PAZ. *Amer. Journ. Physiol.*, 1911, XXVIII, 64.
- <sup>4</sup> ELLIOTT. *Journ. Physiol.*, 1912, XLIV, 374.
- <sup>5</sup> EMBLEY. *Brit. med. Journ.*, 1902, I, 817, 885, 951.
- <sup>6</sup> GARREY. *Amer. Journ. Physiol.*, 1908, XXI, 283.
- <sup>7</sup> GASKELL. *Schäfer's Physiology*, I, 1900.
- <sup>8</sup> HEIDENHAIN. *Arch. f. d. ges. Physiol.*, 1872, v, 143.
- <sup>9</sup> HERING. *Arch. f. d. ges. Physiol.*, 1900, LXXXII, I.
- <sup>10</sup> HUNT. *Amer. Journ. Physiol.*, 1899, II, 395.
- <sup>11</sup> KAHN. *Arch. f. d. ges. Physiol.*, 1909, CXXXIX, 379.
- <sup>12</sup> KIRK. "A New Theory of Chloroform Syncope," Glasgow, 1890; *Lancet*, 1893, II, 428.
- <sup>13</sup> KNOLL. *Sitzungsb. d. Akad. d. Wissenschaft. z. Wein*, 1872, LXVI, 143.
- <sup>14</sup> LEVY. *Proc. physiol. Soc.*, Jan., 1911, *Journ. of Physiol.*, XLII, iii.
- <sup>15</sup> LEVY. *Proc. physiol. Soc.*, Oct., 1911, *Journ. of Physiol.*, XLIII, xviii.
- <sup>16</sup> LEVY. *Proc. physiol. Soc.*, May, 1912, *Journ. of Physiol.*, XLIV, xvii.
- <sup>17</sup> LEVY. *Lancet*, 1905, I, 1413.
- <sup>18</sup> LEVY. *Brit. med. Journ.*, 1912, II, 627.
- <sup>19</sup> LEVY. *Brit. med. Journ.*, 1906, II, 242.
- <sup>20</sup> LEVY. *Proc. roy. Soc. Med.*, 1910-11, IV (pathol. section), 205.

---

\* The term "irritability" of the heart has been generally employed in this paper to denote a tendency to the exhibition of beats of heterogenetic origin.



- <sup>21</sup> LEVY AND LEWIS. *Heart*, 1911-12, III, 99.
- <sup>22</sup> MACWILLIAM. *Journ. of Physiol.*, 1887, VIII, 296.
- <sup>23</sup> MACWILLIAM. *Brit. med. Journ.*, 1890, II, 831, 890, 948.
- <sup>24</sup> REIGHARD AND JENNINGS. "Anatomy of the Cat," 1901, London.
- <sup>25</sup> ROTHBERGER AND WINTERBERG. *Arch. f. d. ges. Physiol.*, 1911, CXLII, 461, and previous volumes.
- <sup>26</sup> SHERRINGTON AND SOWTON. *Brit. med. Journ.* (Reports of the Special Chloroform Committee), 1903, Supplement, CXLVII, 1904, II, 162.
- <sup>27</sup> SNOW. "On Anæsthetics," 1858, London.
- <sup>28</sup> SOLLMAN AND PILCHER. *Amer. Journ. Physiol.*, 1910, XXVI, 238.
- <sup>29</sup> VON ANREP. *Journ. of Physiol.*, 1912, XLV, 318.
- <sup>30</sup> WILSON. *Lancet*, 1894, II, 1148; 1897, II, 656; 1898, II, 260.

### *Appendix.*

Additional reports of clinical cases which illustrate the points dealt with in the body of the paper.

(1) A case illustrating non-fatal cardiac syncope occurring in the course of an operation.

This case occurred in my own experience when I was practising anæsthetics some years ago; my own form of chloroform inhaler was being employed.

"Female aged 55. Operation for large mammary carcinoma.

Put under chloroform very quietly and gradually, reaching a maximum of 3 per cent.

Incision made at 3 per cent.; a faint corneal reflex and slight expiratory phonation being evident at the time.

The index was very soon put back to 2 per cent., and maintained there, pupil being small; colour, and breathing good.

During the stripping of the tumour the pupils became a little bigger, about 2.5 mm. in diameter, and the colour paler, and the vapour was reduced to 1.5 per cent. in consequence; but as the colour did not improve and the corneal reflex was found absent, the inhalation was then stopped. Shortly after this the pupils were noticed to be very dilated, and the pulse absent, but the breathing remained good and unobstructed.

The patient was placed in the 'feet-up' position, when the breathing ceased.

Chest compression quickly caused the breathing and pulse to return.

The operation was resumed at 1 per cent., the pulse again became faint during the clearing of the clavicular glands.

Total time of operation: Forty-four minutes, the pulse being excellent at the finish."

(*Proc. roy. Soc. of Medicine*, Vol. II, Part I.)

This patient was very carefully watched from the commencement for symptoms of overdosage, and there was nothing to suggest that anything was wrong until the tumour was being stripped off the muscles; on the onset of pallor in accordance with the accepted teaching at this time the chloroform was at once reduced, and subsequently entirely removed, with an almost fatal result. As I would now judge, the pallor and slight dilatation of the pupils were both evidences of a reflex sympathetic action with probably a co-existing ventricular tachycardia, and an indication for keeping up a full degree of anæsthesia; the result of stopping the inhalation entirely was a progression to ventricular fibrillation which fortunately was of temporary duration only. I reported this case as an instance of how the most careful regulation of the chloroform will not obviate a form of cardiac shock, but I did not at the time appreciate how near this patient came to death.

(2.) This case is taken from the Final Report of the Special Chloroform Committee of the British Medical Association. The regulating inhaler employed was of the Vernon Harcourt type.

"Female aged 31, who suffered from exophthalmic goitre.

The anæsthesia was devoid of any abnormal phenomena, and death, which occurred when the thyroid tumour was being drawn from its attachment, was sudden and of the cardiac type, no doubt arising from 'vagal inhibition.'

The patient was anæsthetic, but not profoundly narcotised at the time of collapse, 0.5 per cent. was being inhaled."

(Supplement to the *British Medical Journal*, July 29th, 1910, p. 63.)

(3.) A case reported by myself some years ago. It illustrates the form of death by intermission and re-application in the induction period. The signs of imperfect anæsthesia were abundantly evident up to the moment of death, and it was this case, observed in January, 1906, which first induced me to seek for some explanation of sudden death apart from that generally accepted, *i.e.*, overdosage.



"Male, aged 47. Weight 15 st., fat and flabby, pasty complexion.

Under treatment for diabetes, 2·2 per cent. of sugar in the urine (total sugar not recorded).

Proposed operation, removal of big toe for necrosis; administration by Dr. Levy's inhaler, complete anaesthesia induced in seven minutes, with a maximum vapour of 1·8 per cent.

A delay now ensued in consequence of the theatre not being ready, and the patient was allowed to come round a little, when he commenced to vomit, and the facepiece had to be removed and cleaned. There was subsequently cause for expedition, and the inhalation was continued at 3 per cent., but as the breathing was restrained and embarrassed by a tendency to retch, he failed to go under.

Suddenly the type of breathing changed, the respirations becoming very deep and forcible; not more than six or seven of these respirations had been taken when the pupils were found to be widely dilated, the face very pale, and radial pulse imperceptible. Respiration quickly ceased. Fitful attempts at spontaneous respiration were produced by appropriate treatment, but the heart never recovered."

(4.) This case is taken from Snow's book and is a report by Mr. Paget of the death of a boy of nine years occurring at St. Bartholomew's Hospital in 1856. The first page of the report relates to the induction which was irregular and prolonged, and this I have omitted.

"I was on the point of commencing the operation, but as he again, by movements, indicated some degree of sensibility, and changed his posture, about forty drops more of chloroform were poured on cotton wool, inclosed in a fold of lint, an inhaler, with the chloroform on a sponge, having been previously used. The lint was held, about half an inch from the face, by Mr. Thomas Smith, my usual assistant in operations. The patient inhaled lightly for a few times, then made one long inspiration, and appeared to pass at once into deep sleep. Except that he thus appeared to come suddenly under the full influence of chloroform, no external change was visible; but, a few seconds later, his pulse, which had been carefully watched, and had been to this time normal, suddenly began to beat very quickly; then it ceased for two or three seconds; then beat rapidly several times, with a kind of flickering movement; and then ceased to be perceptible.

Just before this change of the pulse was observed, the chloroform had been withdrawn. The one deep inspiration was followed by a few stertorous breathings, but after these he breathed naturally, his complexion and features showed no change, he seemed only calmly asleep, and in this state he continued breathing naturally, and with no change in his appearance, but pulseless, for at least a minute. Then his breathing became less frequent, and seemed as if it might soon cease; his face grew pale, and his lips very slightly livid.

I refrain, at present, from all comments on this case. Only, I wish to call particular attention to the fact that good breathing was maintained, and, after a suspension, was renewed, long after the heart had ceased to act with sufficient force to produce a pulse at the wrist. And I would add, that this narration is sanctioned and considered to be exact, by the four gentlemen who were to have assisted in the operation, and to whom I am greatly indebted for their counsel and assistance in the greater difficulty that we had to cope with."—*Medical Times and Gazette*, 1856, Vol. I, p. 236.

This abstract is given here mainly on account of the description of the condition of the pulse which preceded death, and which is a vivid word picture of the irregular condition shown in some of my pressure curves.

It is not quite clear from the text whether withdrawal of the chloroform or its re-application immediately preceded death, but both these procedures are mentioned.

"(5). Woman, aged 49. Pale and thin.

Anæsthetic: Chloroform, 2 drachms; a little ether added towards the end of induction. Induction gradual, by drops on open mask, held all the time about an inch from the face. Some slight irritative coughing at first in spite of very gradual administration. This ceased and there were slight muscular movements of the limbs and a little muttering; no struggling. Respiration quiet and regular. Lips and ears very good colour. Pupils medium, corneal reflex brisk. Then sudden alteration in breathing (five minutes after beginning of induction). There were seven or eight deep sighing respirations, and at the same moment wide dilatation of the pupil, pulse disappeared, no pallor for ten or fifteen seconds. Then cessation of respiration (no respiratory embarrassment at all before the sudden collapse). Tongue pulled forward, artificial respiration, oxygen, strychnine, &c. No further sign of life.

The symptoms came on a very few seconds after a fairly brisk corneal reflex had been obtained, only a few drops had been added, the mask was always a little off the face."

Judging by the final remarks death would appear to be due to a re-application, "only a few drops," probably (and this can only be surmised) after an intermission; the description of method is of the usual vague nature. The degree of anæsthesia was carefully noted; it was of a light description, and the mode of death from sudden primary cardiac failure is evident. There can be no other explanation of this death but that of ventricular fibrillation.—*Proc. roy. Soc. of Medicine*, Vol. 5, No. 2 (Section Anæsthetics.)



# THE INFLUENCE OF INCREASE OF TEMPERATURE UPON THE INHIBITORY MECHANISM OF THE HEART OF THE MAMMAL.

BY G. H. CLARK.

(*From the Department of Physiology, University of Glasgow*).

IN a paper published in 1912<sup>3</sup> the author showed that in the heart of the frog the activity of the vagus was markedly diminished when the temperature was raised somewhat above that of the animal. It was further shown that the part of the heart which was acted upon in this way was the sino-auricular junction at the part known as the crescent.

A metal point warmed to a known temperature was applied to various points on the surface of the heart and at this part only was it effective in diminishing the inhibitory action of central stimulation of the vagus.

The work detailed in this paper was undertaken with the object of finding if this condition applied equally to the mammalian heart.

## *Historical.*

The earlier work upon the frog's heart is considered in the previous paper. Baxt<sup>1</sup> first recorded a series of observations upon mammals. In the dog he found the inhibitory action of the vagus remained unchanged between 26° and 39° C..

Schiff,<sup>7</sup> on the other hand, found that in rabbits the activity of the vagus was diminished on warming the heart to 37° or 38° C..

Lauder Brunton,<sup>2</sup> also using rabbits, concluded that "in the heart of the rabbit, and probably other mammalian hearts, a temperature sufficiently high to produce stoppage of the heart does not paralyse the vagus or the inhibitory apparatus through which it acts." Lauder Brunton's protocols show something more than this. He remarks earlier in his paper "from these experiments, and especially from No. VIII, it will be seen that as the temperature was raised and the pulse quickened the power of the vagus diminished." The return of activity took place just before the heart was brought to a standstill by the increased temperature. These higher temperatures reached 47° C., and in most of the experiments recorded the vagus was shown to be less active at temperatures between the normal and the extreme high temperature. Howell, Budgett and Leonard,<sup>6</sup> examining the influence of diminution of temperature upon the activity of the vagus, found that the rabbit reacted differently to the dog, and it is a question whether this fact does not account for the discrepancy in the results described. The previous work on the subject is meagre and, in view of these different results arrived at and the conclusive results obtained by me in the case of the frog, the question requires further investigating.

## *Present Investigation.*

In the work here described, the contractions of the right auricle and the ventricle were recorded.

A tracheal cannula having been inserted and the vagi exposed, ligatured and cut, the skin was removed from the anterior surface of the chest. A cut was then made through the muscles covering the seventh and eighth ribs on the right side of the chest and the ribs divided. The forefinger of the left hand was next inserted through the opening in the chest wall thus made. Artificial respiration was used after this stage in the experiment. Using the left forefinger as a director it was found possible to extend the opening in the chest wall up to the third rib without damaging the lung. The forefinger was next moved round underneath the sternum and the internal mammary arteries compressed. The sternum was then cut across below the finger without loss of blood. The opening into the thorax was continued round to the left side and carried up to the third rib on that side. A large flap of skin, muscle and bone was then reflected upwards, tightly ligatured at its proximal end, and cut off. The heart in the pericardium was thus exposed without loss of blood. The pericardium was next slit open and clipped to the chest wall with bulldog forceps. A small spring clip was attached to the right auricle and another similar one to the right ventricle. These spring clips were connected by threads carried over pulleys, with frog-heart levers writing on a smoked drum. When an alteration in temperature was desired saline solution or Ringer's solution at the desired temperature was poured down a funnel on to the heart or into the thoracic cavity. The fluid filled the thorax and overflowed into a receptacle placed below.

In a small number of experiments at the beginning of the series, a cannula was inserted into the carotid artery and the trace of the blood pressure recorded without making a large opening in the chest wall. Here alterations in temperature were obtained by placing a hot rubber bag upon the chest wall and reading the temperature upon a thermometer placed deeply within the thorax. This method was subsequently abandoned owing to its uncertainty. In nearly all cases the same procedure was adopted in making observations. The secondary coil was drawn out until a stimulus was found which was subminimal. The coil was now pushed in until a definite result was produced on stimulating the vagus. The heart was now warmed to the required temperature and the above procedure repeated. The animal was next left for some minutes until the temperature of the heart again became normal and the effect of stimulation of the vagus with the same and different strengths of stimulation recorded.

In the great majority of experiments rabbits were used, but in addition several cats and three dogs were used in endeavouring to arrive at a definite conclusion as to the influence of increase of temperature upon the activity of the vagus.

The temperature to which the heart was raised varied between  $40^{\circ}$  and  $43^{\circ}$  C. but was generally  $40^{\circ}$  or  $41^{\circ}$  C., being a rise of about  $2^{\circ}$  to  $3^{\circ}$  C.<sup>4</sup> above normal, and consequently a temperature which might be attained during a febrile attack.

In most experiments the left vagus was stimulated, although in some the right or both were made use of.



*Results.*

In considering the results of these experiments, the rate of the heart and its amplitude have been taken as a measure of the effect of vagal stimulation. Unless otherwise stated, reference is made to the left vagus. In the first series, where the blood pressure trace alone was recorded, a fall in blood pressure was taken as a measure of the activity of the nerve.

In the rabbits the results were generally in support of Schiff's statement that the vagus was less active at temperatures somewhat above normal.

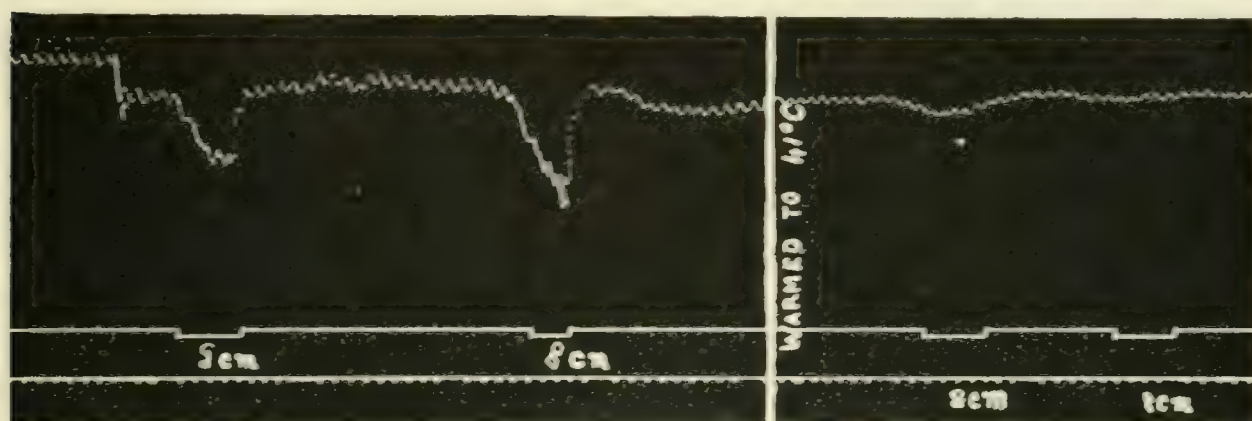


Fig. 1. Influence of increase of temperature upon the activity of the vagus. Traces of the blood pressure. 1 With the normal temperature, stimulation with the secondary at 8 cm. twice gave marked fall in blood pressure. On warming the heart, stimulation with the secondary at 8 cm. twice failed to cause a fall in blood pressure. All tracings read from left to right.

Where the blood pressure curve was recorded, if there was a definite fall with a certain strength of stimulus in the normal heart, that strength of stimulus produced a lesser effect or no effect on the pressure tracing when the temperature was raised.

This is shown in Fig. 1. Here stimulation of the left vagus with the secondary coil 8 cm. distant from the primary, gave a fall in blood pressure, which was more marked when repeated.

When the heart was warmed by a hot rubber bag being placed on the chest until the thermometer in the thorax registered  $41^{\circ}\text{C}$ ., stimulation of the vagus with the same strength of stimulus gave a very small fall in pressure the first time and no fall the second time of application.

In most of the experiments the temperature was allowed to return to normal and the reaction again tested.

When the heart was exposed and tracings taken the results were in most cases striking.

In one experiment, typical of many, when the vagus was stimulated with the secondary at 10 cm., inhibition of the whole heart resulted. Both auricular and ventricular rate and amplitude were affected. When the stimulation was repeated with the secondary at 12 cm. some slowing occurred after about three seconds and diminution in amplitude of the auricular trace.

The heart was now warmed to  $40^{\circ}\text{C}$ . and the vagus again stimulated as before. With the secondary at 12 cm., there was no change in the rate of the auricular or ventricular contraction, although the alternately larger

and smaller contractions of the ventricle, slightly noticeable before stimulation, became more marked after three seconds. With the secondary at 10 cm., stimulation made this irregularity still more marked, as did stimulation with the secondary at 8 cm., where some degree of slowing also occurred. Stimulation with the secondary at 6 cm. caused standstill of both chambers with escape beats in the auricle.

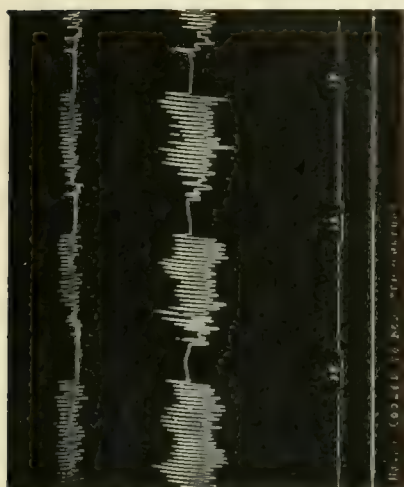
The heart was now allowed to return to its normal temperature and stimulation of the vagus repeated as before. With the secondary at 12 cm., standstill was obtained in the ventricle and marked slowing in the auricle. With the secondary at 14 cm., stimulation caused slowing of the auricle and a primary augmentation of the ventricular contraction followed by inhibition and periods of standstill. The heart was again warmed to 40° C. and the alternate large and small contractions again appeared, but these were lost on stimulating the vagus with the secondary at 14 cm.. Stimulation with the secondary at 12 cm. caused no slowing of the heart, but the irregularity again became as marked as before. Repetition of the stimulation with the secondary at 10 cm. caused standstill of the ventricle and a marked slowing of the auricle. Cooling again to normal, stimulation of the vagus with the secondary at 10 and 12 cm. gave standstill of the whole heart. Stimulation at 14 cm. gave slowing of the whole heart and short periods of standstill in the ventricle. Stimulation with the secondary at 16 cm. gave slowing and augmentation.

Fig. 2 shows records taken during a prolonged experiment. With the heart at the normal temperature stimulation with the secondary at 13, 14, 15 and 16 cm. gave standstill of the whole heart with escapes in the first case. Stimulation at 18 cm. gave slowing of the heart. The heart was now warmed to 40° C. and stimulation at 18 and 16 cm. did not alter the heart beat, but stimulation at 15 cm. caused standstill of the whole heart with an escape beat on the auricular trace. The temperature was brought to normal and the vagus stimulated with the secondary at 15, 16, 17, 18, 19 and 20 cm., and standstill of the whole heart obtained. Very marked slowing was obtained with the secondary at 21, 22, 23, 24 and 25 cm.. The heart was now warmed to 40° C. and stimulated as before. 15, 16, 17 and 18 cm. gave standstill, 20 cm. gave marked slowing of the whole heart, and 21 cm. twice gave no result. The heart, again cooled to normal, was brought to standstill with a stimulus of 22 cm. strength, and was very markedly slowed with stimuli of 23, 24 and 25 cm. strength while 26 cm. had no great effect. It will be noticed that at the beginning of the experiment the first sign of inhibition appeared when, with the secondary at 18 cm., a slight degree of slowing was obtained when the left vagus was stimulated. After warming to 40° C., and again cooling, stimulation with the secondary at 18, 19 and 20 cm. gave standstill of the whole heart and inhibition was obtained with the secondary at 25 cm.. This increase of sensitiveness of the heart to vagus stimulation was marked in very many of my experiments. This is also well shown in the experiment given in detail earlier in this paper, where a strength of 14 cm. caused standstill of the ventricle at the end of the

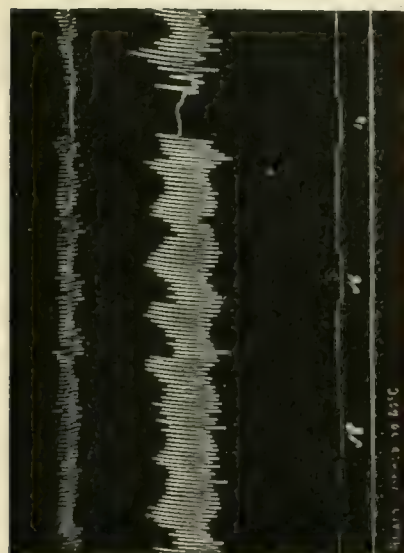


Fig. 2. Influence of increased temperature upon the activity of the vagus.

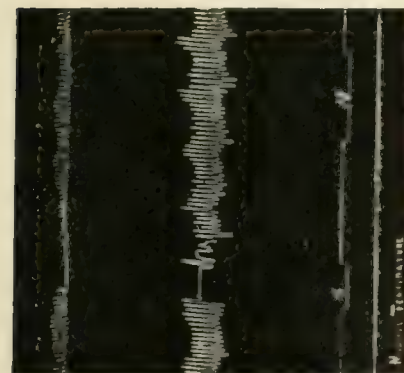
1. With heart at normal temperature secondary at 16 cm. gave standstill, 18 cm. gave slowing. 2. After warming to 40°C. 18 and 16 cm. gave no result, but 15 cm. gave standstill. 3. After now cooling to normal, stimulation with secondary at 15, 16, and 17 cm. gave standstill. 4. Continuous stimulation after cooling, 18, 19 and 20, gave standstill and 21 cm. gave inhibition. 5. With still weaker stimuli, 22, 23, 24 and 25 cm. inhibition was obtained. 6. The heart was now warmed to 40°C. and stimuli obtained with secondary at 15, 16, 17 and 18 cm. secondary obtained standstill. 7. With the heart still warmed stimulation with secondary at 20 cm. gave marked slowing in ventricle, but 21 cm. gave no result. 8. Heart now cooled for two minutes, stimulation with secondary at 22 cm. gave standstill—23, 24, 25 cm. gave inhibition.



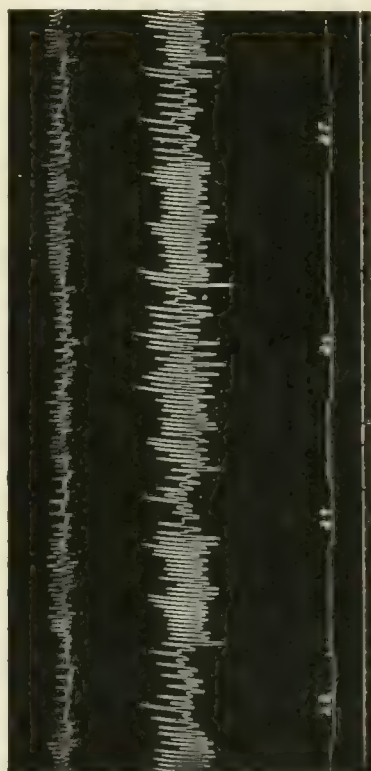
3



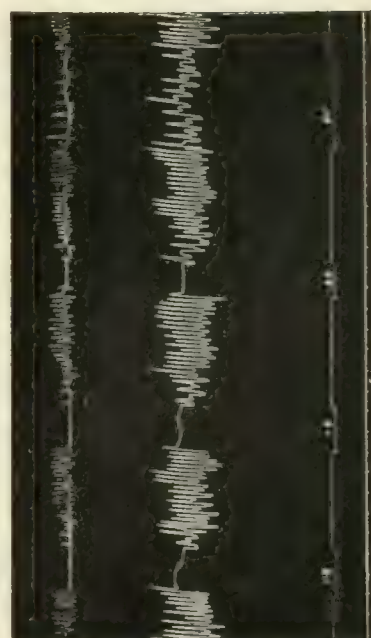
2



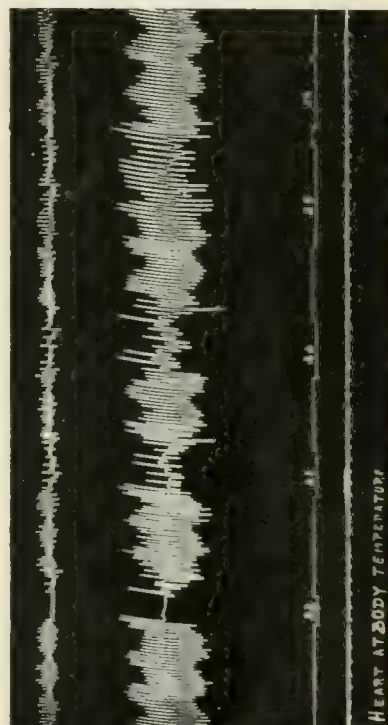
1



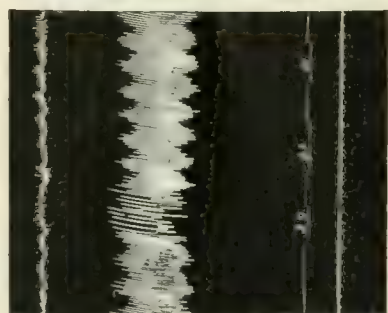
5



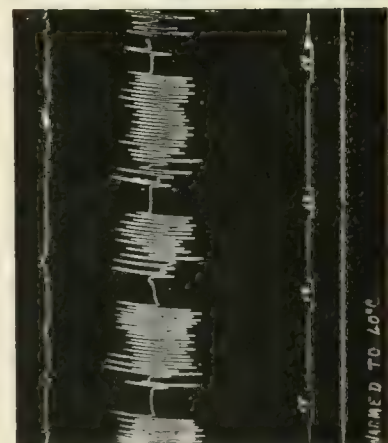
4



8



7



6

experiment, whereas a strength of 10 cm. was required at the beginning. Many such might be quoted.

Where dogs were used the results were not constant, and a further series of experiments requires to be done. Cats, generally, reacted in the same way as rabbits.

For the purpose of testing whether the nature of the fluid used for warming the heart played any part in inhibiting the activity of the vagus as suggested by Hagan and Ormond,<sup>5</sup> experiments were performed in which both Ringer's solution and normal saline solution were used with the same heart. It was found here that the same results were obtained with either solution. Where the warm saline solution caused a very marked change in sensitiveness of the vagus, warm Ringer's solution did the same. Where the influence of the Ringer's solution was not great, then saline had no greater effect.

A small number of experiments were performed in which a von Frey's temperature point heated to the desired temperature was applied to different parts of the heart's surface in the endeavour to localise the seat of this action of increased temperature as was done in the frog. These experiments were not successful, probably owing to the more diffuse distribution of the primitive cardiac tissue in the sinus end of the mammalian heart. This work is still being proceeded with.

#### SUMMARY.

Experimental evidence is brought forward to prove that in the rabbit, as in the frog, increase of temperature by three or four degrees C. diminishes the sensitiveness of the heart to vagus stimulation. This was not marked in the dogs that were examined, but appeared to be the case also in cats.

This diminished effect of vagal stimulation during increased temperature is followed by an increased effect *after* the temperature has returned to normal. An attempt to localise the particular part of the heart which was thus affected by increased temperature was not successful. The same results were obtained whether saline solution or Ringer's solution was used, and similar results were obtained in some early experiments where a hot rubber bag was applied to the chest wall and the temperature read upon a thermometer thrust deeply into the thorax.

(A grant from the Carnegie Trust was received to defray the expenses of this research.)

#### BIBLIOGRAPHY.

- <sup>1</sup> BAXT. Ludwig's Arbeiten, 1875, x, 179.
- <sup>2</sup> BRUNTON. Bart's Hosp. Reports, 1871, vii, 216.
- <sup>3</sup> CLARK. Journ. of Physiol., 1912, XLIV, 169.
- <sup>4</sup> FROTHINGHAM AND MINOT. Amer. Journ. of Physiol., 1912, xxx, 430.
- <sup>5</sup> HAGAN AND ORMOND. Amer. Journ. of Physiol., 1912, xxx, 105.
- <sup>6</sup> HOWELL, BUDGETT AND LEONARD. Journ. of Physiol., 1894, xvi, 298.
- <sup>7</sup> SCHIFF. Archiv. f. d. ges. Physiol., 1878, xviii, 172.



## LESIONS OF THE BRANCHES OF THE AURICULO-VENTRICULAR BUNDLE.

BY GEORGE D. MATHEWSON.

*(From the Clinical Medicine Research Laboratory of the Royal Infirmary, Edinburgh).*

THE experimental work of Eppinger and Rothberger<sup>4</sup> has proved that a lesion dividing one or other branch of the auriculo-ventricular bundle produces marked and characteristic changes in the electrocardiographic curves obtained from the heart. Comparison of curves obtained clinically, with those published in the record of their experiments, has enabled some observers since to make the diagnosis of lesion of one or other branch, and in a few cases the diagnosis has been confirmed post-mortem. In the four cases here described, such confirmation is necessarily lacking, as all are still alive. They illustrate well, however, varying degrees of myocardial involvement and show how the site of the lesions can be deduced with a fair degree of certainty from the electrocardiograms obtained.

### *Obstruction of the right branch of the bundle.*

CASE 1. A. P. Man aged 67. Repeated attacks of rheumatic fever in early life. Syphilitic infection denied. Suffers from dyspnoea and oedema of feet and legs. Heart much enlarged. Systolic apical murmur. Vessels markedly thickened. Systolic pressure 210 mm. Hg. Pulse rate about 90 per minute with occasional irregularity. Urine contains a trace of albumin but no casts.

In this case (Fig. 1-4) the ventricular complexes exhibit the form which, from experimental and clinical experience, is regarded as indicating conduction of stimuli by the left branch only.<sup>4 & 5</sup> The broad initial upward deflexion and the subsequent downward deflexion by derivation *I* (Fig. 1), and the opposite effect by derivation *III* (Fig. 2) are well marked. The curves resemble very closely those from one of Eppinger and Stoerk's cases (Fig. 5 and 6 in their paper<sup>5</sup>) in which complete interruption of the right branch of the bundle was found post-mortem. Derivation *II* gives a complex resembling that of derivation *III* rather than that of derivation *I*. Records obtained by derivations *I V* and *V* showed curves closely resembling those obtained by derivations *II* and *III* respectively.

Conduction by the main stem and left branch of the bundle must be intact, for each auricular complex is followed, at the normal interval, by the ventricular. Another indication of the functional integrity of these parts of the bundle is the fact that stimulation of the vagus by pressure does not constantly cause any dropping out of ventricular beats as it would tend to do were there any latent defect of conductivity in them.<sup>10 & 11</sup>

The obstruction in the right branch is evidently of a permanent nature, for records obtained on two occasions over five months apart show precisely similar curves.

*Obstruction of the mainstem and right branch of the bundle.*

*CASE 2.* Man aged 37. Stokes-Adams syndrome.

The patient was brought to the infirmary on one occasion to have electrocardiograms taken. No further clinical notes are available.

The records of this case (Fig. 5-7) show complete dissociation of auricle and ventricle. Ventricular contraction is rhythmic, and the rate is 28 per minute. The ventricular complexes are of abnormal form. It may be stated with certainty that in this case there is a lesion which involves some part of the main stem of the bundle and causes the complete block. It is probable that there is also a lesion in the right branch which produces the abnormal form of ventricular complex. If the lesion were confined to the main stem, the ventricular complex would be of the form associated with beats of supraventricular origin. If the main stem were intact and both branches obstructed, complete dissociation would be present but one would expect the ventricular complex to have the peculiar form which has been proved to occur when conduction is interrupted in both branches.<sup>3 & 4</sup> The case resembles in nature one recently reported by Cohn and Lewis<sup>2</sup> in which lesions in the main stem and right branch of the bundle were found at autopsy. The ventricular complexes in the case here described seem even more distinctly removed from the normal form than in their case. This may possibly depend upon the branch lesion being here more complete in nature.

*Transient obstruction in the left branch of the bundle.*

*CASE 3.* H. D. Man aged 46. Rheumatic fever 17 years ago. Has recently suffered from dyspnoea and palpitation on exertion. Some oedema of the feet. Cyanosis. Pulse is rapid and shows total irregularity. Vessels rather thickened. Heart greatly enlarged. No murmur audible. Urine contains a little albumin.

This case displays (Fig. 8) normal ventricular complexes (A) occurring in groups with abnormal complexes (B) interspersed. As the record is obtained by derivation *I*, the abnormal ventricular form suggests that which is regarded as indicating conduction by the right branch of the bundle



only.<sup>4</sup> It seems as though some slight lesion of the left branch may be present, interfering now and again with conduction through it. As the auricles are fibrillating and there is thus no *P* deflexion in the record, it is uncertain whether the abnormal ventricular complexes have arisen in response to supraventricular stimuli. They may conceivably be extrasystolic beats of the type usually regarded at present as basal or right sided.<sup>6 & 7</sup> On this view the lesion is not an obstructive one but rather an irritative one probably affecting some part of the muscle of the right ventricle or its conduction system.

*Transient obstruction occurring alternately in the two branches of the bundle.*

**CASE 4.** J. P. Man aged 57. No history of rheumatic or syphilitic infection. Admitted to hospital suffering from dyspnoea on exertion. Subsequent hæmoptysis. Lung bases congested. Heart dilated. Apical systolic murmur. Vessels thickened. Systolic pressure 110 mm. Hg. Pulse very irregular at times.

If the records of this case (Fig. 9-14) are examined, neglecting meanwhile the premature beats and confining attention to those of the auricular rhythm, it will be seen that they seem to furnish evidence of various methods of conduction of the stimulus to the ventricles. Fig. 9, by derivation *I* shows normal conduction by both branches, giving a normal ventricular complex(A). Fig. 10 by derivation *III*, Fig. 11 by derivation *II*, and Fig. 12 by derivation *III* all show complexes suggestive of left branch conduction (B). Fig. 13 by derivation *III* shows left branch conduction (B) passing into complexes (C) which, while abnormal in respect of the inversion of *T*, are not apparently inconsistent with conduction by both branches. Fig. 14 by derivation *I* shows two varieties of ventricular complex. The one (D) is obviously abnormal with the main deflexion directed downwards suggesting right branch conduction. The other (E) which has its main deflexion upwards, while more nearly approaching the normal form, presents certain differences from the normal complexes shown in Fig. 9 and obtained by the same derivation. It should probably be regarded as an abnormal form indicative of left branch conduction. The auricular deflexion is not well marked in this figure but is probably present in its normal position relative to the ventricular, for it is clearly shown in Fig. 12 obtained on the same occasion by a different derivation. We have then in this case stimuli apparently conducted at times by the right branch, at times by the left branch, and sometimes normally by both branches simultaneously. This is the case whether the doubtful complexes (E) of Fig. 14 are regarded as normal or not. To explain the occurrence of the various methods of conduction exhibited in this case, lesions affecting both branches of the bundle must be postulated. These cause only a temporary suspension of function, for each branch takes its turn in conducting the stimulus to the ventricles and both are at times functioning together.

*Extrasystoles associated with lesion of the branches of the auriculo-ventricular bundle.*

*CASE 1* and *CASE 4* exhibit, in some of the records, extrasystoles interrupting the physiological rhythm. Figs. 3 and 4, both from *CASE 1*, show two distinct forms of extrasystole. In Fig. 3, by derivation *II*, an auricular extrasystole (Ex.) is seen. The ventricular complex is identical with that of the other beats, while the auricular deflexion is of anomalous form, indicating the probable origin of the stimulus in some other part of the auricle than the sino-auricular node.<sup>8</sup> In Fig. 4, by derivation *II*, two ventricular extrasystoles are seen. They are of the type usually described as apical or left-sided.<sup>6 & 7</sup> These premature beats afford evidence of further myocardial damage in addition to the lesion of the right branch already described. Foci of irritation are present in the auricle and probably in some part of the left ventricle. Extrasystoles appear in all save one of the records from *CASE 4*. In Fig. 11, by derivation *II*, the premature beats which do not open the aortic cusps, are of apical or left-sided type. There is evidence of disturbed auricular rhythm, the notch on the beginning of the final upward deflexion of the premature beats, probably representing auricular activity. Fig. 12, by derivation *III*, shows one premature beat (R) of the basal type and one (L) of the apical. In Fig. 13, by derivation *III*, the second element in each couple is a premature beat of apical form. Two types of these are seen. In the premature beats (X) following the complexes of left branch conduction (B) the deflexions from the base line are comparatively slight, while in those (Y) following the normal complexes (C) the deflexions are much more marked and more typical of apical stimulation. Both forms appear to be associated with premature auricular contractions, the evidence of which is similar to that described in Fig. 11. In Fig. 14, by derivation *I*, a single premature beat occurs, it is of basal or right-sided type.

This case presents evidence of irritation of the ventricular muscle at more than one point, for the records show basal extrasystoles and possibly two varieties of apical. In discussing the conduction lesions the conclusion was reached that there must be a lesion in each branch of the bundle. While the precise site of origin of the extrasystoles cannot be determined with any certainty, it seems reasonable to suppose that the lesions involving the bundle branches may be at once obstructive and irritative and that the premature beats may arise in the neighbourhood of these lesions and so, in this sense, be truly right-sided and left-sided extrasystoles.

*General remarks.*

In their account of experimental division of the bundle branches in the dog, Eppinger and Rothberger<sup>4</sup> state that they have observed the onset of a gallop rhythm after division of one branch. This they attribute to a loss of synchronism in the action of the two ventricles. The initiation of activity in the chamber to which conduction is imperfect is supposed to be delayed.



Eppinger and Stoerk<sup>5</sup> state that they have detected gallop rhythm in one case of two in the human subject in which the existence of a lesion in the right bundle branch was established post-mortem, and indicate that they have observed the same rhythm in cases presenting electrocardiograms suggestive of similar lesions. On the other hand Barker and Hirschfelder<sup>1</sup> found that after experimental division of one branch, the activity of the ventricles, as mechanically recorded, was quite synchronous. In none of the four cases which I now describe could gallop rhythm be detected.

As regards the relative frequency of obstruction of the two branches of the bundle, it may be pointed out that in three of the four cases here described, the right branch seems to be affected, while it is not quite certain which branch has suffered in the remaining case, *CASE 3*. In only one case, *CASE 4*, are the appearances suggestive of left branch obstruction and this appears to be incomplete. No general conclusions can, of course, be drawn from so few cases, but it is noticeable that in most of the published electrocardiograms when a single branch has been obstructed it is the right branch which is affected. This might be anticipated upon anatomical grounds for the right branch is the more slender and compact, while the left branch spreads out, almost from the commencement, in a broader, more extended form. A comparatively small lesion may thus interrupt conduction in the right branch.

Hitherto all the published accounts of cases in which conduction by one bundle branch has been interrupted have shown the condition to be a permanent feature of the case. Very recently, however, Lewis<sup>9</sup> has described and published electrocardiograms of a case in which the functional defect in the right branch of the bundle is of transient nature. His case displayed left branch conduction one day and normal conduction on the following day. A similar condition is seen in *CASE 4* of my series but, as shown in Fig. 13, both conduction methods are actually displayed in the same record. A similar state of affairs appears in Fig. 14 where there is, I believe, evidence of conduction first by one branch and then by the other.

#### SUMMARY.

The action of the heart is studied, in four cases, by means of Einthoven's string galvanometer. All the cases display alterations in the electrocardiographic curves, which, in the present state of our knowledge, may be regarded as indicating interference with the normal stimulus conduction in the branches of the bundle.

*CASE 4* illustrates transient interruption of conduction in the branches, a phenomenon which has been only once previously recorded. The records of this case are unique in actually showing the occurrence of the change in the method of conduction.

Single extrasystoles appear in some of the records, suggesting that myocardial irritation exists along with the obstruction. Gallop rhythm does not occur in any of the cases.

I have, in conclusion, to acknowledge the kindness of Sir R. W. Philip and of Dr. William Russell, who permitted me to make observations upon patients in their wards in the Royal Infirmary.

## BIBLIOGRAPHY.

- <sup>1</sup> BARKER AND HIRSCHFELDER. Trans. Assoc. Amer. Physicians, 1909, xxiv, 313.
- <sup>2</sup> COHN AND LEWIS. Heart, 1912-13, iv, 7.
- <sup>3</sup> COHN AND LEWIS. Heart, 1912-13, iv, 15.
- <sup>4</sup> EPPINGER AND ROTHBERGER. Zeitsch. f. klin. Med., 1910, lxx, 1-20.
- <sup>5</sup> EPPINGER AND STOERK. Zeitsch. f. klin. Med., 1910, lxxi, 157.
- <sup>6</sup> KRAUS AND NICOLAI. Berl. klin. Wochenschr., 1907, xliv, 765 and 811.
- <sup>7</sup> KRAUS AND NICOLAI. Deutsch. med. Wochenschr., 1908, xxxiv, 1.
- <sup>8</sup> LEWIS. Heart, 1910, ii, 23.
- <sup>9</sup> LEWIS. Brit. med. Journ., 1913, i, 484.
- <sup>10</sup> RIHL. Zeitsch. f. exper. Pathol. u. Therap., 1905, ii, 83.
- <sup>11</sup> VOLHARD. Deutsch. Archiv. f. klin. Med., 1909, xcvi, 348.



of 4  
the

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig.

Fig. 12.

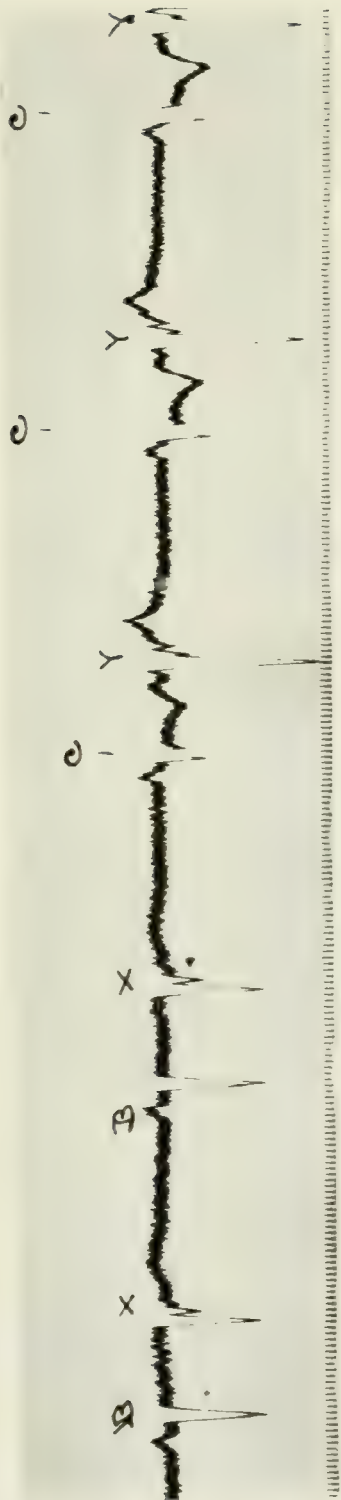


Fig. 13.

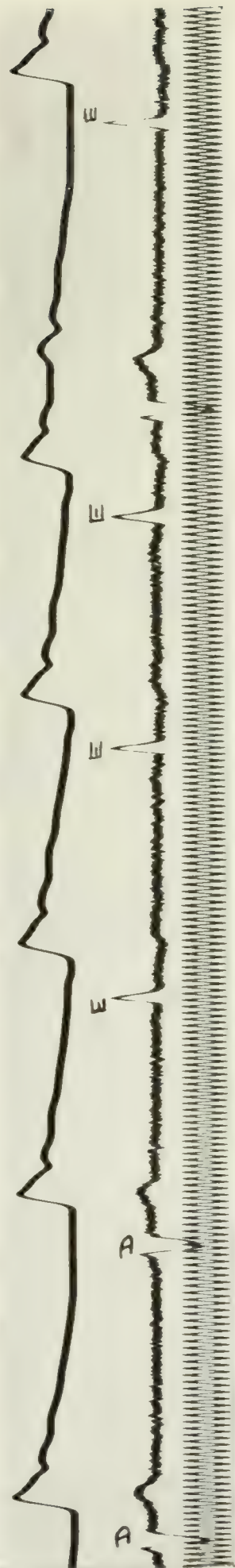
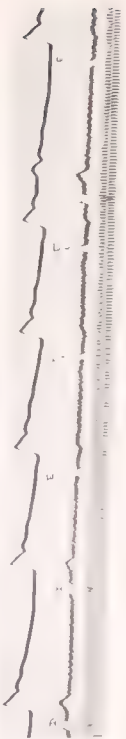
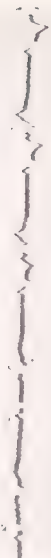
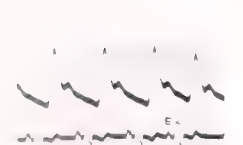
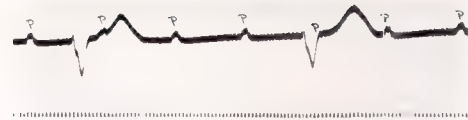
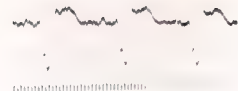


Fig. 14.





## THE CONDUCTION OF THE PULSE WAVE AND ITS RELATION TO THE ESTIMATION OF SYSTOLIC BLOOD-PRESSURE.

By J. A. MACWILLIAM, J. E. KESSON, AND G. SPENCER MELVIN.

*(From the Physiological Laboratory of the University of Aberdeen).*

THE conduction of the systolic wave along the arteries is obviously a matter of much importance in relation to the estimation of blood-pressure by the obliteration method. We have evidence that the condition of the blood-vessels in the limbs may profoundly influence blood-pressure readings and the indications of aortic pressure, so that very different readings may be got from different limbs of the same person at the same time, and from the same limb after continued or repeated compression. Such might conceivably be due to various causes—altered conduction, resistance of the arterial wall to compression or reflection from the periphery. It is highly important to ascertain the importance of these possible factors. Great importance has been attached by some investigators to the influence of altered conduction of the systolic wave along the arterial tube.

It is clear that rigid tubes from the aorta would give the most accurate rendering of the internal pressure. The arm and leg arteries serve as tubes leading from the aorta, tubes of varying degrees of elasticity. In the normal state they give readings that are practically similar in arm and leg in the horizontal position. Evidently the loss from the aorta is similar in both cases, whether it be small or great. The loss might conceivably be great in both in the normal state. The readings would then show no absolute value as regards the aortic blood-pressure, but would have a certain relation to aortic pressure, which would remain constant as long as the essential conditions remain unchanged. We know that sometimes there are great differences between arm and leg readings, and between the readings from the two arms, apparently due to altered local conditions—changes in the conditions of the arteries in the limbs. It is plain that a departure from normal conditions may occur in the arm as well as in the leg. There seems no reason why contraction or other alteration in the arm arteries should not give high readings like those of the leg. May high arm readings be thus got without actual change in the aortic pressure? In cases of wide discordance between the readings from different limbs, it is obviously essential to ascertain which is the approximately correct guide to aortic pressure. If better conduction of the systolic wave in a more contracted or more rigid artery, *e.g.*, in the leg, is the cause, then the leg reading is more nearly correct, and the aortic pressure is vastly higher than the arm reading indicates. This would mean a very great loss in transmission from the aorta to the arm.

On the other hand, if resistance to compression is the sole or main cause of the higher leg readings,\* then these readings are obviously excessive and are much further from being a true indication of the actual blood-pressure than the arm readings. The same is true if reflection from the periphery exercises an important influence in the leg.\*

In the present investigation we have sought to ascertain the behaviour of the arteries as regards conduction in different conditions of relaxation, contraction, increased rigidity, &c. There are two ways in which altered conditions of the arteries might conceivably affect conduction of the systolic wave. First, by alterations in the rigidity or resilience of the arterial wall, modifying the propagation of the wave; and, second, alterations in the lumen, the wave being possibly cut down in its transmission along a narrowed tube.

#### METHODS.

We have performed very numerous experiments on artificial circulation schemas and on the circulation of animals and men. We have employed three forms of schema giving a pulsatile flow at rates like those of the human pulse, and pressures at various levels, from those of high blood-pressure down to very low pressures. Ringer's fluid was used as the circulating medium. The systolic wave was obtained in different ways in the schemas. First, a Higginson's syringe worked by a water motor was used. Second, a rotating tap worked by an electro-motor was interposed between an elevated reservoir and the tube leading to the artery. Third, an electro-magnetic interrupter was interposed instead of the rotating tap. The peripheral resistance to the outflow from each system was obtained :—

- (1) by using a tube drawn out to a point as an outlet ;
- (2) by elevation of the outlet tube without constriction, and
- (3) by a spring outlet.

The pressures were varied by :—

- (1) altering the rate of pulsation ;
- (2) altering the height of the reservoir or altering the stop-cock between the reservoir and the artery, or in the case of the Higginson's syringe, by modifying the extent of compression at each beat, and
- (3) changing the peripheral resistance to outflow from the system.

Wide variations of pulse pressure range were tried.

---

\* There is no evidence of this under the conditions of the clinical estimation of blood-pressure, though, as is well known, higher systolic pressures have been recorded under experimental conditions in the femoral artery than in the carotid.



We have used different kinds of arteries—the carotids of the sheep, ox and horse, and the metacarpals of the horse. To test an extreme case of distensibility and resilience (beyond what is possible in the human arteries concerned in blood-pressure estimation) we have often employed the relaxed carotid of the ox, a large and highly expansile tube showing extensive pulsatory changes at low diastolic pressures—elongation, transverse expansion, &c. We have always used arteries of lengths equal to or greater than that of the arterial trunk leading from the aorta to the seat of brachial compression in ordinary blood-pressure estimation in man. Rubber tubes, differing much in their properties from arteries, are unsuitable for experiment in this connection.

### TYPES OF EXPERIMENTS.

The following types of experiments were employed, the results being compared in the three schemas.

#### *Experiment 1.*

A piece of artery 10-12 cm. long (*e.g.* relaxed carotid of sheep) was enclosed in a compression tube like that already described in a former paper,

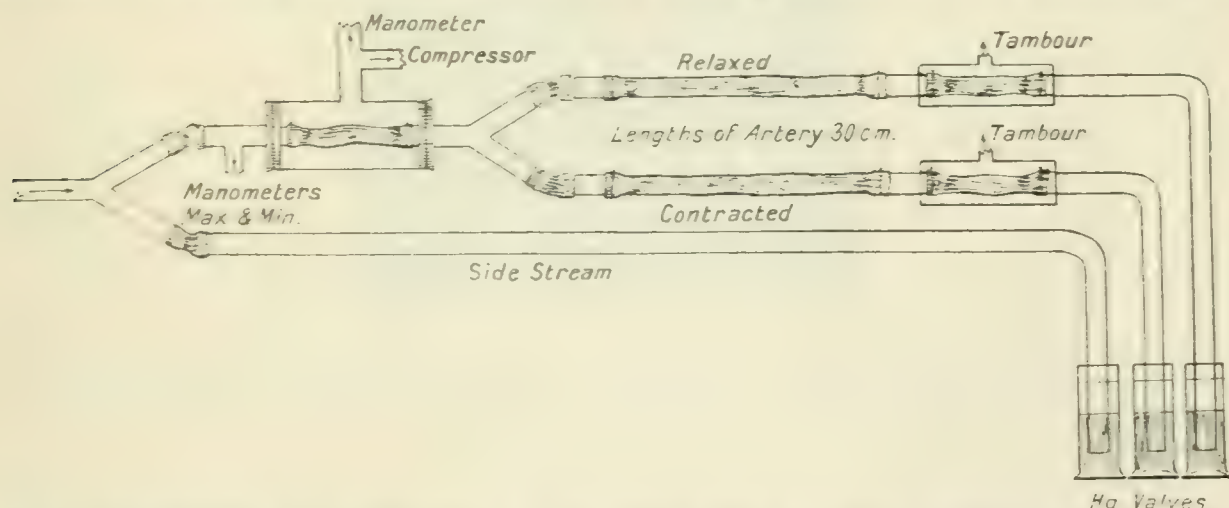


Fig. 1. Arrangement of Experiment 1. The test pieces of carotid (sheep) are here shown enclosed in small plethysmographs; sometimes instead of this arrangement, levers were made to rest on the arteries, or direct inspection, or the tactile method was used. The bent tubes dipping into the Hg. were quite short and of equal length; their lengths are unequally rendered in the drawing. Each tube ends in a separate Hg. valve; otherwise pulsation might in certain circumstances be propagated through the Hg. from one tube to another.

so that obliteration could be effected by raising the external pressure as indicated by a mercury manometer, while the internal pressure was ascertained by valved manometers on the proximal side of the compression tube. The glass tube leading out from the artery in the compression tube branched so that it was possible to interpose on the stream a length of artery, contracted or relaxed, and to compare the transmission of the pulse wave along these. Lengths of about 30 cm. (carotid of ox, &c.) were commonly used. Distally to these lengths of artery a short piece of relaxed carotid (sheep) was interposed to allow the presence or absence of pulsation to be tested in the

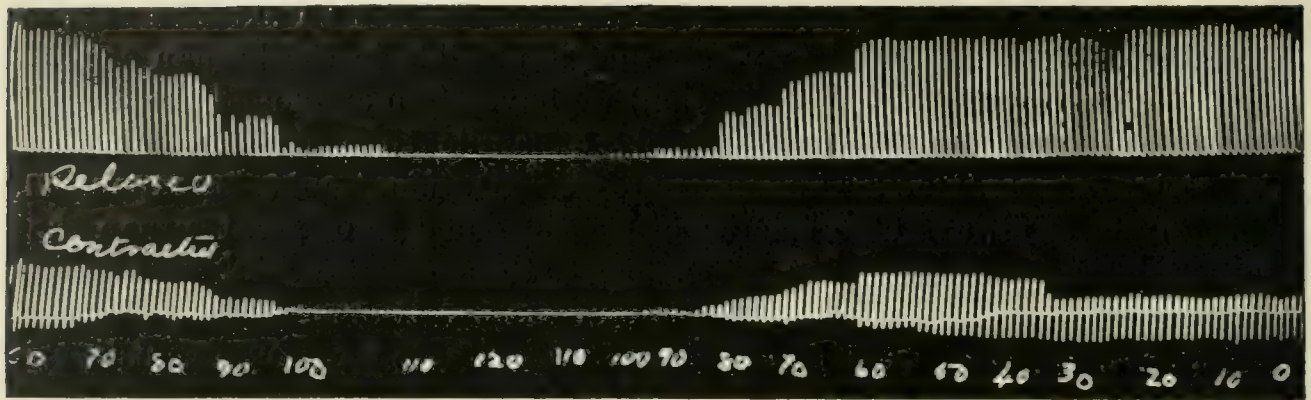


Fig. 2. Pulsation transmitted through relaxed (upper tracing) and contracted (lower tracing) arteries, recorded by levers as stated in the description of Experiment 1. The obliteration of the pulsation, caused by raising the external pressure in the compression tube, is seen to occur pretty equally in both; there is complete obliteration in both at 120 mm. The numbers beneath the lower tracing indicate the external pressures—compressing the piece of artery—in the compression tube. To be read from left to right, as also are the tracings in Fig. 3 and 4.

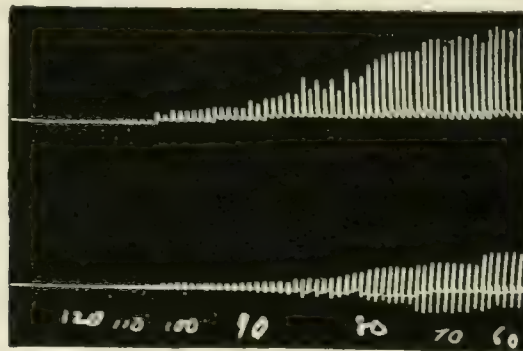


Fig. 3. Shows the recommencement of pulsation after complete obliteration in another experiment. The upper lever is in relation with the relaxed and the lower with the contracted artery.

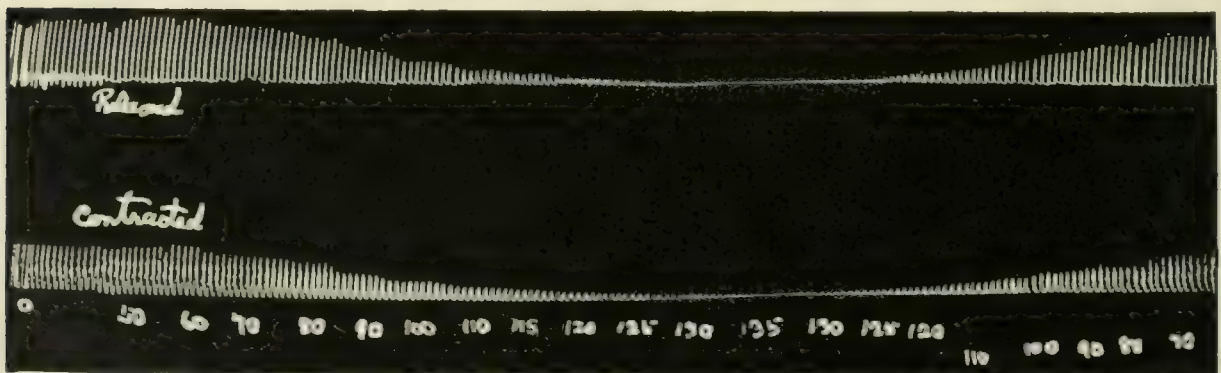


Fig. 4. Pulsation transmitted through lengths of relaxed and contracted arteries as in Experiment 1, recorded plethysmographically. The upper tracing relates to the relaxed and the lower to the contracted artery. When the external pressure in the compression tube is raised to 135 pulsation is almost abolished in both records, there being no recognisable difference in its manifestation after passing through the lengths of relaxed and contracted artery respectively. The numbers beneath the lower tracing show the external pressures in the compression tube in mm. Hg.



two streams. (See Fig. 1). The external pressure around the artery in the compression tube was gradually raised, and obliteration of the pulse was ascertained in the two test pieces of sheep's carotid. Various methods were used to determine the points of abolition and return of pulsation in these pieces—(a) the ordinary tactile method, (b) direct inspection,\* (c) the use of levers resting on the artery, (d) and enclosure of the pieces of arteries in plethysmographs. The recording mechanisms thus obtained were interchanged from time to time, as it was sometimes found impossible to obtain absolute equality in sensitiveness as far as graphic records were concerned. The outflow from the arteries was regulated (a) by Hg. valves as shown in Fig. 1, or (b) by turning up the (open) ends of the tubes to a certain level, or by simply allowing a free outlet at table level without resistance. In this way the influence of different residual pressures, after the artery in the compression tube had been obliterated, was tested.

It was found by the various methods employed that the propagation of the systolic wave was not appreciably different in the lengths of contracted and relaxed artery through which it had passed. (See Fig. 2, 3 and 4.) The disappearance and reappearance of the pulse in the test pieces of sheep's carotid varied only in trivial degree, even when low residual pressures—down to 0—beyond (*i.e.*, distally to) the seat of obliteration were used. When a glass tube of calibre similar to that of the relaxed artery was compared with the latter, the difference between the two was quite inconsiderable.

Similar lengths of rubber or glass tubing were also tried in place of the contracted and relaxed arteries and tested in the same ways; the transmission was found to be similar in the two tubes.

In some experiments the contracted and relaxed arteries were examined separately, one only being placed on the stream at a time, the branched glass tube being replaced by a simple one. In this way any possible disturbance from the presence of streams of very unequal volume through the contracted and relaxed arteries was avoided. Similar results were got.

In a number of cases observations were made by watching the movement of the levers resting on the test pieces of sheep's carotid—instead of making them record graphically. In this way possible inequalities of friction at the writing points were avoided, though fallacy from this cause was also obviated by interchanging the recording mechanisms from time to time. An example of the nature of the results obtained is subjoined.

Visual examination of levers, weighted but not writing on drum. The external pressure in the compression tube was raised sufficiently to cause obliteration and then allowed to fall so as to test disappearance and reappearance of the pulse in the streams passing through the contracted and relaxed arteries respectively. The residual pressure in the tubes (arteries, &c.) distal to the compression tube when obliteration was effected in the latter was 10 mm. Hg.—measured by an Hg. manometer, connected on the distal side of the compression tube and not shown in Fig. 1. The peripheral resistance determining the residual pressure was provided in this experiment by

---

\* Direct inspection showed the presence of pulsation somewhat below the point at which the tactile index ceased, as also did inspection of the levers when not inscribing on the drum.

elevating the ends of the outlet tubes to a suitable height. The lever connected with the length of relaxed artery is designated R; that with the contracted artery C.

External pressure in compression tube.

140 Just perceptible movement of R.

No perceptible movement of C.

138 Somewhat more marked movement of R.

Just perceptible movement of C.

136 Decided movement in both, somewhat more pronounced in R.

Residual pressure reduced to 3 mm. Hg.

Levers not weighted.

136 Both stopped.

132 „ moving.

140 „ stopped. Systolic pressure somewhat raised.

136 „ moving.

138 „ „ faintly.

Lengths of contracted and relaxed artery interchanged.

Levers not disturbed, but their relations to the contracted and relaxed arteries are reversed.

132 Both moving about equally.

134 „ just moving.

136 „ stopped.

134 „ moving perceptibly—about equally.

One artery used at a time.

Contracted.

140 Perceptible movement.

141 No movement.

Relaxed.

138 Perceptible movement.

140 No distinct movement.

138 Perceptible movement.

### *Experiment 2.*

Here a considerable stretch of relaxed artery, *e.g.*, 30 cm. of ox carotid, was placed on the stream distally to the compression tube, with a test piece



Fig. 5. To test conduction along a 30 cm. length of artery (relaxed, &c.), the latter was placed distally to the compression tube with short pieces of relaxed carotid (sheep) near each end. A lever rested on each of these pieces and was made to record graphically or its movement was watched for cessation and recommencement of the pulse when the external pressure in the compression tube was raised to obliteration point and lowered. The relaxed carotid of the ox or horse, a large resilient tube, was often taken as the 30 cm. length.

of relaxed carotid (sheep) at each end. On each of these pieces a lever was made to rest. (See Fig. 5.) This lever was made to record in the usual way, or its movement was examined by direct inspection; sometimes the piece of artery was watched for visible pulsation without a lever, or the usual tactile index was employed. When the artery in the compression tube was obliterated by a gradual rise of external pressure, the distal lever stopped moving sooner than the proximal one, indicating a certain loss in transmission along the 30 cm. length of relaxed carotid, but this loss was always



inconsiderable, amounting only to such values as 4-8 mm., very low residual pressures (down to 0) being tried in some cases. There was a slight loss even when a contracted artery or a glass tube was used in similar circumstances.

The evidence obtained from these two forms of experiment shows very little effect of contraction and relaxation in influencing the propagation of the systolic wave under those conditions. They quite oppose the idea of any extensive damping down of the wave in its passage along the relaxed tube.

These types of experiment bear more directly upon the propagation below the armlet in ordinary blood-pressure estimations, between the brachial artery and the radial. In order to compare more closely the conditions obtaining in blood-pressure estimations as regards the behaviour of the arterial tube proximal to the armlet, between the armlet and the aorta, we have carried out other experiments.

### Experiment 3.

Here the artery was placed on the stream between proximal and distal manometers connected as shown in Fig. 6,\* or in other cases, in such a way

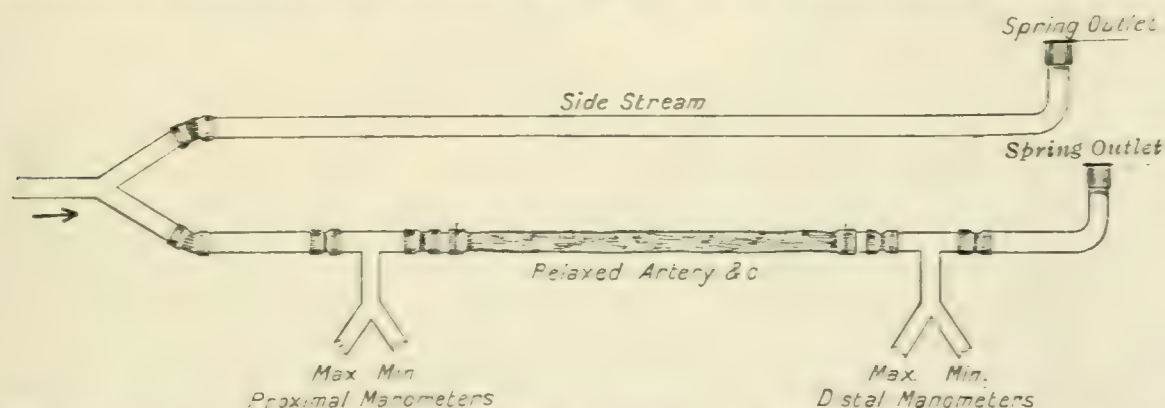


Fig. 6. To test conduction in a length of relaxed artery (or glass tube). Valved manometers are connected near the proximal and distal ends of the artery. The peripheral resistance is supplied by spring outlets—a broad flat spring (faced with india-rubber) closing the enlarged mouths of the discharge tubes. (The enlargement of the mouth is not shown.)

that the manometer connections faced the stream. Lengths of contracted and relaxed artery were used and also similar lengths of glass tubing of various calibres. Calibre was found to exert a very important influence under conditions of this sort, there being a great loss in transmission along a narrow tube, *e.g.*, with a 1 mm. tube the distal pressure was cut down enormously; with a 3 mm. tube, to a less extent, but still greatly. When a length of relaxed artery was compared with the contracted artery, various results were obtained, depending upon the inter-action of two factors, (a) the difference in rigidity of the arterial walls, and (b) the size of the lumen. The

\* In this type of experiment, as in some others, we have supplied peripheral resistance by using a broad flat spring faced with india-rubber to close the widened mouth of each outlet tube and resist the outflow of fluid. With some forms of peripheral resistance (*e.g.*, a tube drawn out to a point) reflected waves occur, causing the systolic pressure to be higher in the distal than in the proximal manometer.

resultant of these factors was such that often little difference was found in the transmission of the systolic wave in the contracted and relaxed arteries. (The systolic pressure in the whole system is naturally lower when a large resilient relaxed artery is included in it.)

Relaxed arteries were also compared with rigid tubes of similar calibre, and it was found that the relaxed artery showed a loss commonly of from 5 to 10% as compared with the rigid tube, the loss being greater with very free outflow and very low diastolic pressures.

#### *Experiment 4.*

Arteries in different conditions and rigid tubes of different calibres were tested by being placed between the proximal manometers and the stream, in the way shown in Fig. 7. The influence of calibre was here found to be

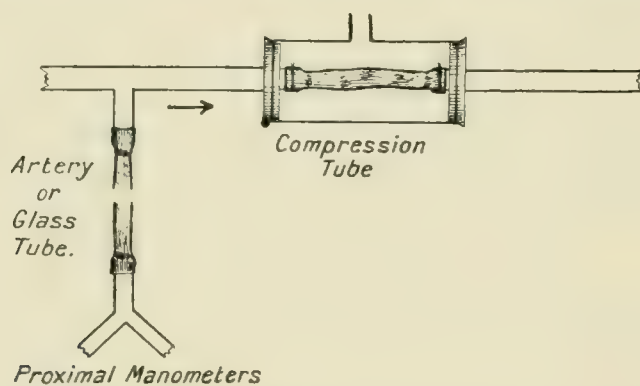


Fig. 7. Arrangement for testing the conduction of the systolic wave in a piece of artery or in tubes of various calibres interposed between the stream to the compression tube and the proximal manometer. Manometer and obliteration give corresponding readings.

slight. With the stream flowing, there was no appreciable difference when 3 mm. and 1 mm. tubes were compared. When the stream was stopped by obliteration of the artery in the compression tube, there were differences commonly of about 4 or 5% in favour of the larger tube. Still larger tubes gave no difference as regards systolic pressure. Relaxed arteries show no appreciable difference as compared with glass tubes of similar dimensions, as far as systolic pressure is concerned—no appreciable loss in conduction.

The systolic pressure within the system was tested by ascertaining the external pressure necessary to obliterate the artery in the compression tube, as shown by disappearance and reappearance of the pulse distally to the compression tube. The values ascertained in this way were compared with the simultaneous readings of the proximal manometer (maximal) when a relaxed or contracted artery or glass tubes of various calibres were interposed between the manometers and the stream; they agreed in each case.

Of course the systolic pressure in the system was lower when a large relaxed artery was used—on account of the elasticity thus added to the system, but the measurement of such pressure by the manometer was not appreciably affected by the presence of the large resilient tube on the way to the manometer. The obliteration test, just referred to, shows this.



*Experiment 5.*

The arteries to be tested in different conditions and the rigid tubes of different calibres were placed between the proximal manometer connection and the compression tube (as shown in Fig. 8). Beyond the compression

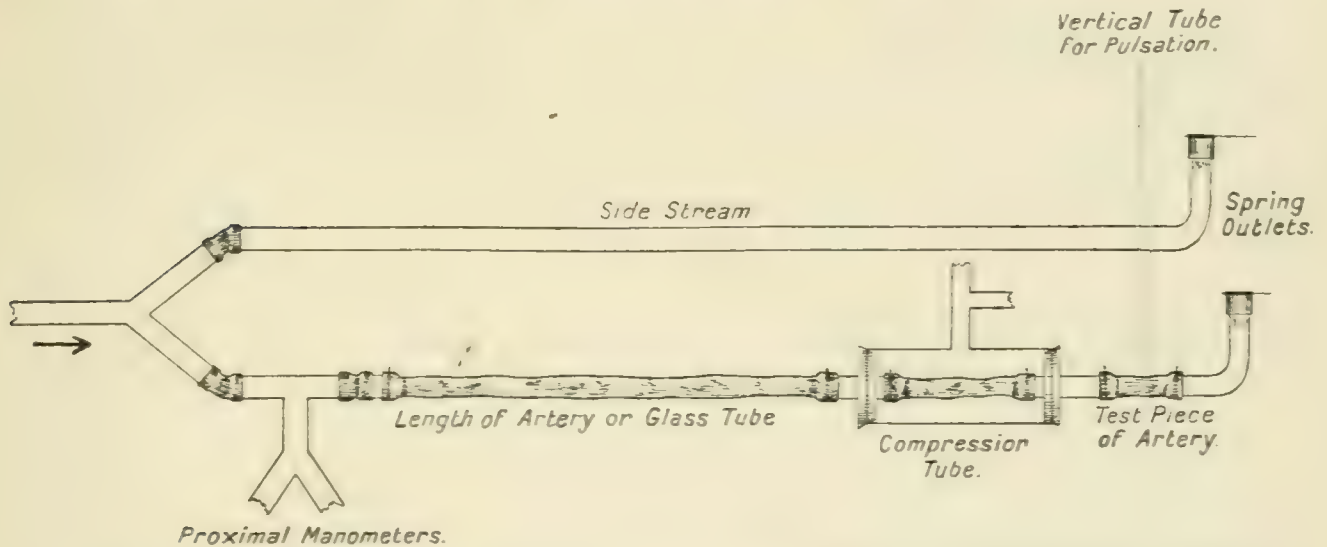


Fig. 8. To show the arrangement used in Experiment 5. The vertical glass tube mentioned in the text is indicated by dotted lines.

tube a test piece of relaxed artery was placed to detect the disappearance and re-appearance of the pulse in the usual ways—tactile, visual, lever, &c., or instead of these test pieces a vertical glass tube was connected to serve as an indicator of the pulse.\* No appreciable difference was obtained with equal lengths of relaxed and contracted artery at ordinary diastolic pressures, *e.g.*, 50-70, and sometimes not even with diastolic pressures as low as from 10 mm. down to 0 with systolic pressures of 50, &c. The same held good when the relaxed artery was compared with a glass tube of similar calibre.

While the systolic pressure was lower in the whole system with a large expansile or relaxed artery there was no evidence of loss in transmission along the resilient tube, as tested by obliteration on the distal side.

The influence of calibre was tested with rigid tubes, 10-22.5 cm. in length and 1 mm. and 3 mm. in calibre; with the 1 mm. tube losses were found varying according to the conditions present, from 5 to 15%.

These results are obviously opposed to the idea of a great loss occurring in systolic propagation from aorta to brachial. But in the latter the conditions are not quite identical in this respect, that, in the experiment just described, there is a stationary column of fluid between the obliterated artery and the manometer connection where the measurement of pressure is made, whereas in man there is a certain amount of flow along the arterial tube between aorta and obliterated brachial, the blood passing out by the

\* The side stream indicated in Fig. 8 obviates the occurrence of any great change in the systolic pressure when obliteration is effected in the compression tube.

various branches of the subclavian, axillary, and the part of the brachial above the seat of compression. In order to reproduce this condition more closely, we have used the next mentioned form of experiment.

### Experiment 6.

Here a modification is introduced for the purpose just stated, by interposing an additional outlet at the distal end of the length of artery being examined, *i.e.*, between the end of the artery and the compression tube, as shown in Fig. 9. This provides for a certain amount of flow through the

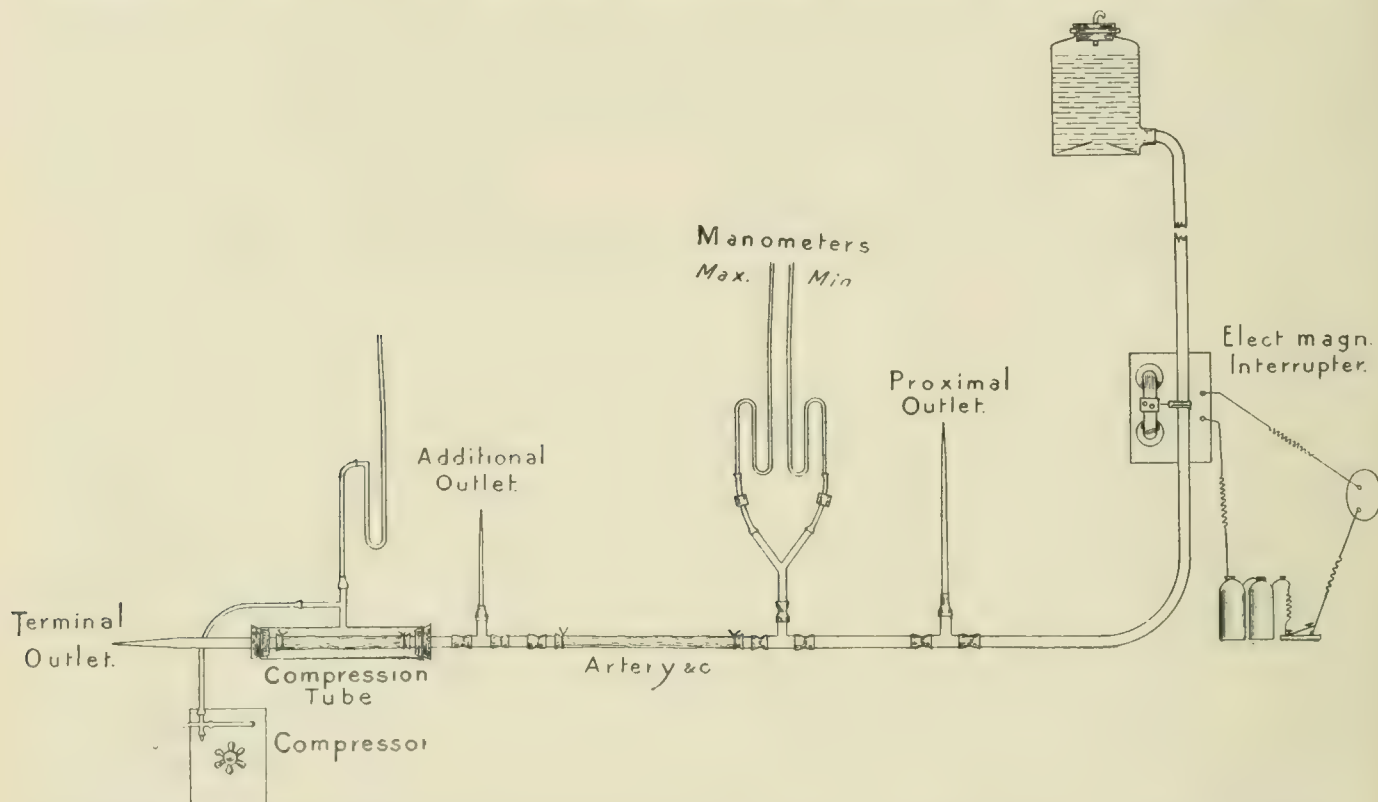


Fig. 9. Arrangement for testing conduction along an artery placed before the compression tube, a certain amount of flow being allowed to continue through the artery (by the additional outlet) while obliteration is tested in the usual way by raising the external pressure in the compression tube. The electro-magnetic device for rhythmically interrupting the stream (60 times per minute, &c.) from the reservoir is described elsewhere. (*This Journal*, IV, 279.)

length of artery when obliteration has been effected in the compression tube. It was found that no important effect resulted from this modification, when relaxed artery and rigid tube of similar calibres were compared as before.

When rigid tubes of extremely small calibre were used, a certain effect was produced, though it was not very extensive and the diminution of calibre required to produce such effect was so great, *e.g.*, 1 mm., that it does not seem to have any application to the conditions present in blood-pressure estimation in man by the obliteration method applied to the brachial artery—in view of the large size of the arterial trunk leading from the aorta to the brachial. Constriction of the main artery would, no doubt, be accompanied by constriction—probably more extreme—of its branches and a diminished flow through them—*caeteris paribus*.



*Experiment 7.*

An arterial cannula in the abdominal aorta or carotid (cat) was connected with a branched tube leading to lengths of relaxed artery and rigid tubing, each of which conducted to maximal and minimal manometers, as indicated in Fig. 10. It was found that similar readings were obtained in both sets of

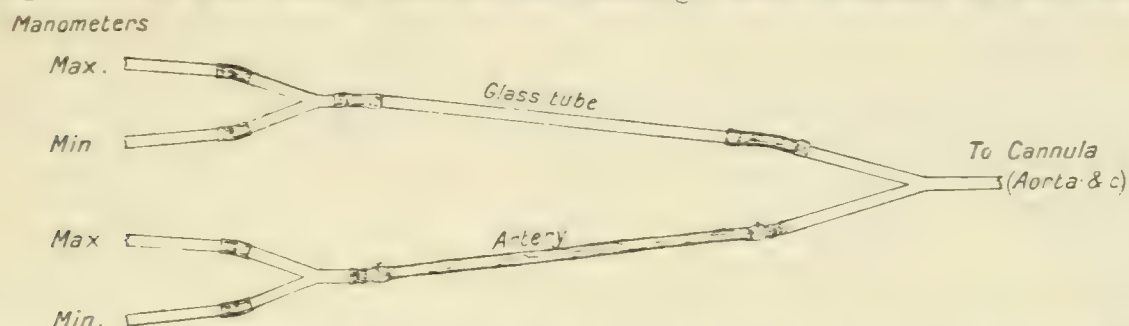


Fig. 10. To show the mode of simultaneously testing conduction through a relaxed artery 27-30 cm. long (carotid of sheep) and a rigid (glass) tube of similar dimensions placed on the way from the aorta or carotid to the pairs of valved manometers.

manometers, both as regards systolic and diastolic pressures. Evidently the transmission of the pressure was not appreciably different in the relaxed artery and the rigid tube. This held good at very different levels of pressure in different experiments, or in the course of the same experiment. Such differences were introduced in various ways by vagus stimulation, by the administration of amyl nitrite, chloral, &c. Systolic pressures varying from 118 mm. to 18 mm. and diastolic pressures ranging from 110 mm. to as low as 10 mm. were observed, and in every case, whether with slow or fast pulse rates, the manometer indications varied in similar fashion. The resilience of the relaxed artery was obviously in play though not showing any appreciable result in the readings; very marked pulsation was evident in the artery—locomotion, bending and transverse expansion—at the lower diastolic pressures.

The manometer readings were of course made simultaneously, and were checked by different observers.

A few examples are subjoined, obtained from cats anæsthetised with chloroform and chloral. The pulse-rates were as a rule very fast and the pulse-pressure range relatively small, though not always so. Sodium citrate solution was used as an anti-coagulant in the blood-pressure cannula.

*Experiment A.*

Blood-pressure cannula in carotid. Lengths of glass tubing and relaxed carotid (sheep) 27 cm. long on the way to the manometers.

| SYSTOLIC.                       |                 | DIASTOLIC.  |                 |
|---------------------------------|-----------------|-------------|-----------------|
| GLASS TUBE.                     | RELAXED ARTERY. | GLASS TUBE. | RELAXED ARTERY. |
| 118                             | 118             | 110         | 110             |
| 114                             | 114             | 100-104     | 102-104         |
| Heart slowed somewhat by vagus. |                 |             |                 |
| 80                              | 80              | 72          | 72              |
| 82                              | 82              | 74          | 74              |
| Amyl nitrate administered.      |                 |             |                 |
| 66-68                           | 66-68           | 60          | 60              |
| Pressure on abdomen.            |                 |             |                 |
| 78                              | 78              | 72          | 72              |
| Later.                          |                 |             |                 |
| 38                              | 38              | 34          | 34              |

*Experiment B.*

In another experiment in which a similar correspondence between the readings was observed (systolics 72 mm. &c.) with a slower pulse and a very much greater range between systolic and diastolic pressures, collapse occurred (overdose of chloroform and chloral) and cardiac massage being employed, the effects of excessively low pressures were observed. Blood press. from carotid.

| SYSTOLIC.   |                 | DIASTOLIC.  |                 |
|-------------|-----------------|-------------|-----------------|
| GLASS TUBE. | RELAXED ARTERY. | GLASS TUBE. | RELAXED ARTERY. |
| 20          | 22              | 12          | 13              |
| 28          | 28              | 12          | 16              |

It is to be noted that even with such extremely low diastolic pressures—bringing out extensive visible pulsation in the length of relaxed artery—there was nothing beyond quite inconsiderable differences—and these rather in favour of the artery.

*Experiment C.*

Blood-pressure from abdominal aorta.

29 cm. lengths of glass tube and relaxed carotid (sheep) used.

| SYSTOLIC.   |                 | DIASTOLIC.  |                 |
|---|-----------------|-------------|-----------------|
| GLASS TUBE.   | RELAXED ARTERY. | GLASS TUBE. | RELAXED ARTERY. |
| 96  | 98              | 84          | 84              |
| 96  | 96              | 80          | 80              |
| 94  | 94              | 80          | 80              |
| Slight vagus stimulation.   |                 |             |                 |
| 84  | 86              | 76          | 76              |
| Amyl nitrite given.   |                 |             |                 |
| 46  | 46              | 40          | 40              |
| Shortly afterwards.   |                 |             |                 |
| 48  | 48              | 44          | 44              |
| 58  | 59              | 50          | 50              |
| Pilocarpine injected.   |                 |             |                 |
| 76  | 76              | 68          | 68              |
| 60  | 60              | 56          | 56              |
| 56  | 56              | 52          | 52              |
| Thorax opened. Heart slowed by<br>faradisation of inhibitory area.      |                 |             |                 |
| 16  | 18              | 10          | 10              |
| Large dose of chloral (intravenous) after<br>faradisation discontinued. |                 |             |                 |
| 30  | 30              | 24          | 24              |

## DISCUSSION OF RESULTS.

*Evidence from the types of experiment described.*

With regard to the two possible factors possibly affecting conduction of the systolic wave (*a*) change in the size of the lumen, and (*b*) change in the character of the arterial wall as regards resilience or rigidity, the foregoing experiments show that in regard to (*a*), constriction of the lumen has very different results according as there is a stream flowing through the tube or not. A tube of small calibre interposed in the course of an actively flowing stream, cuts down the systolic wave very greatly, the amount of diminution varying of course according to the smallness of the calibre, the length of narrow tube interposed, &c. In our experiments the systolic wave was often cut down 50%, &c.

On the other hand, when there is no flow and the narrow tube is filled by a stationary column of fluid leading back to the point where the pressure is measured by the manometer, the effect of smallness of calibre is relatively



slight, amounting to 5-15%, when a very small tube, 1 mm. calibre, of considerable length was used. With a 3 mm. tube no appreciable effect was observed under similar conditions.

When a certain amount of flow through the narrow tube was present, the effects were more marked than in the preceding case, though not very extensive. It is clear that the effects of constriction of the tube under the conditions of blood-pressure estimation by the obliteration method can only exercise any considerable effect when the constriction is extreme—in such a degree as would not be applicable in the case of the arterial tube leading from the aorta to the seat of brachial compression.

Findlay<sup>3</sup> has described the occurrence of very large differences between brachial pressure and digital pressure in certain conditions, *e.g.*, Bright's disease, and also between carotid pressure and paw pressure in cats under the influence of adrenalin. These effects he ascribes to arterial constriction cutting down the systolic wave. Here relatively small arteries are concerned, as compared with the large arterial tube constituting the path from the aorta to the upper arm which is in question in ordinary blood-pressure estimation.

As regards the second factor (*b*), our results make it clear that changes in the character of the arterial wall as regards resilience or rigidity make very little, if any, difference under the conditions of blood-pressure estimation, as far as the transmission of pressure from the aorta to the brachial artery is concerned. Our evidence shows that with very extensive changes in the arterial wall varying from a rigid condition to that of a highly elastic and distensible tube, even with excessively low diastolic pressure, no considerable effect, if any, is produced.

It need hardly be said that the elasticity of the aorta and its branches is of prime importance in affecting the pressures in the vascular system, giving lower systolic and higher diastolic pressures than would be present with the heart pumping into relatively inelastic or rigid tubes. But while the height of the aortic systolic pressure is largely influenced by this factor, the transmission of the pressure from aorta to brachial is not appreciably affected, under the conditions of blood-pressure estimation, by the rigidity or resilience of the intervening tube. This tube constitutes only a very small part of the arterial tree, and its condition will affect the aortic pressure only in proportion to the amount of elasticity which it normally contributes to the arterial system as a whole.

Similarly in the case of a distensible and elastic artery between an arterial cannula and a manometer, if the properties of the artery are such as to have any appreciable effect on the manometer reading, such effect is due to a change of carotid and aortic pressure, not to appreciable loss in transmission from the arterial cannula to the manometer.

Hill with Flack and Holtzmann<sup>6</sup> and with Rowland<sup>5</sup> have obtained results which have led them to ascribe very great importance to the influence of the arterial tube in modifying conduction of the systolic wave and so affecting blood-pressure readings very extensively. They interpret the wide

differences in arm and leg readings in the cases of aortic regurgitation (over 100 mm. sometimes) to an influence of this sort, to the leg arteries being more contracted or more rigid and thus conducting the systolic wave better.\*

If this view is correct, the leg readings would afford more accurate indications of aortic pressure than the arm readings, the aortic pressure really being vastly higher than is indicated in the arm. Such a hypothesis would involve the occurrence of a very great loss in transmission between aorta and brachial, as much as 80 mm., 100 mm. or more in some cases.

The experimental evidence we have adduced is entirely opposed to such an assumption; in our experiments even with diastolic pressures lower than any observed in aortic regurgitation, there has been no appreciable effect in the way of loss in transmission along a highly elastic and distensible artery.

#### *Additional evidence.*

There is also evidence to be adduced from other sources. In the case of the normal arm arteries there is no evidence of any important loss in transmission of the pulse wave from brachial to radial. This is seen when the Erlanger<sup>2</sup> apparatus is used for ascertaining systolic pressure in the way described by its inventor, the systolic index being a sudden rise in the size of the oscillations and a separation of the limbs of the individual curves; this systolic index obtained at the upper part of the arm is only slightly different from the tactile index obtained from the radial pulse. Erlanger puts the difference at 5-15 mm., but this difference possibly depends largely on the arrival of fully developed waves at the wrist being taken as the index. When rudimentary waves are taken, Janeway<sup>7</sup> finds a difference of 2-5 mm.; our own experience coincides with that of Janeway. Oliver<sup>8</sup> finds by his visual index that reappearing waves can be detected at the wrist earlier than by the tactile method—this tending to make the difference between arm and wrist still less. In any case it is clear that the loss is a quite inconsiderable or negligible one.

Similar evidence is obtained by comparing the brachial index near the elbow with the radial index. Very little, if any, loss is recognisable.

Again, when obliteration readings are taken from the arm as high up as possible and compared with those from the forearm as low down as possible, the difference is slight, a few mm., up to about 10 mm. in our experience, showing that between those points the passage of the systolic wave is little affected.

The normal artery evidently conducts so well that little can be gained by an increased rigidity of its walls; this is against the idea that a stiffened artery leading from the aorta to the seat of radial compression might give abnormally high readings simply by better transmission of a normal aortic systolic pressure. The same applies to the leg arteries.

---

\* Russell Wells & Hill have recently emphasised the conductance hypothesis. *Proc. roy. Soc., Series B*, LXXXVI 180 )



If the absence of any considerable loss is due to the tone of the artery there ought to be marked loss on reduction or abolition of that tone. Repeated compression of the arm or of both arm and forearm, necessarily causing relaxation of the artery, makes no appreciable difference in the radial index when brachial obliteration is employed, showing that even when the normal tone is in abeyance the loss in transmission is quite inconsiderable.

Even in aortic regurgitation with its low diastolic pressure and large systolic wave, the difference between arm and forearm reading seems to be quite slight. Mr. J. R. Murray, M.B., has been examining this point and allows us to state the result of his observations in this respect ; he finds only a slight loss, *e.g.*, 10 mm., &c. If there were anything like such an enormous loss as 80 or 100 mm. in transmission from aorta to brachial in cases of aortic regurgitation, there ought obviously to be very marked differences between the upper part of the arm and the lower part of the forearm.

Another piece of evidence is derivable from the consideration of arm and leg pressures in the normal individual. In the standing position these pressures are similar when the hydrostatic difference due to the difference in level between the seats of obliteration in arm and leg is deducted. This was described by Hill and Flack,<sup>4</sup> and our own observations are in agreement with theirs. It seems to us that a deduction not made by Hill and Flack may be drawn from the facts stated—a deduction bearing on the question of conduction. In the standing position the leg arteries are exposed to a very much higher internal pressure than the arm arteries in consequence of the hydrostatic factor, *e.g.*, a pressure of 180 mm. in the leg as compared with 120 mm. in the arm, &c. Consequently the leg arteries must be in a tenser condition, the arterial wall being more stretched by the internal pressure and so rendered less distensible ; or if distension is prevented by increased muscular tone, that again involves markedly diminished resilience. In either case it is clear that the leg arteries must under these conditions act as stiffer tubes than the arm arteries. And if conduction is readily and powerfully influenced by alterations in the character of the arterial wall, the systolic wave should be propagated more effectively from the aorta to the leg, with the result that a higher reading should be obtained, as compared with the arm, than would be accounted for by the hydrostatic difference. This, as we have seen, is not the case.

In the case of the arm arteries no marked effect is recognisable, as regards transmission, when the artery is tensely filled and when it is only poorly filled. Such conditions can be compared when blood-pressure readings are being made from the arm in the usual way. If the obliterating pressure is rapidly pumped up, the artery between the armlet and the wrist is relatively empty, *i.e.*, has very low internal pressure. On the other hand, if the armlet pressure is raised to a little below the obliterating pressure and kept at that level for some time, the whole limb below the armlet will become turgid with blood at high pressure as indicated by a pressure in the veins not much below obliteration pressure in the brachial artery. Here the

artery between armlet and wrist is tensely filled, and yet no marked difference in the radial index is recognisable. The auditory method used at the elbow can be employed in this connection, also the Erlanger systolic index.

Further, there is the fact that quite moderate or low pressures are sometimes obtained with sclerosed and inelastic arm arteries. Such might of course be due to abnormally low aortic pressures, so that though transmission from the aorta might conceivably be unusually good, the arm reading might still be low. That such is not the explanation in some such cases is indicated by the fact that the diastolic pressure is not unduly low, and there is no reason to believe that the aortic systolic pressure is abnormally low.

In a careful examination of the pressures at different parts of the arterial tree, made with valved manometers, P. M. Dawson<sup>1</sup> found in the dog only a trivial fall of systolic pressure between the innominate and the right brachial, *e.g.*, a pressure of 160 mm. in the innominate and 156 mm. in the brachial; he found the average in the left brachial to be the same as in the innominate.

#### CONCLUSIONS.

While the elasticity of the aorta and its branches is of great importance in regard to the systolic and diastolic pressures in the arterial tree—giving lower systolic and higher diastolic pressures than would otherwise be present—the transmission of the systolic pressure from the aorta to the brachial artery is not, under the ordinary conditions of blood-pressure estimation by the obliteration method, appreciably influenced by the resilience or rigidity of the intervening arterial tube.

The differences sometimes observed between arm and leg readings, between the two arms, arm and forearm, &c., are not to be explained by differences in the conduction of the systolic wave from the aorta depending on the character of the arterial tubes in the different limbs, &c.

Diminution in the calibre of an artery, if extreme, may influence the propagation of the systolic wave, but under the ordinary conditions of blood-pressure estimation in the arm this factor is a negligible one.

#### BIBLIOGRAPHY.

- <sup>1</sup> DAWSON. *Amer. Journ. Physiol.*, 1905-6, xv, 244.
- <sup>2</sup> ERLANGER. *Amer. Journ. Physiol.*, 1904, x (Proc. Amer. physiol. Soc., p. 14).
- <sup>3</sup> FINDLAY. *Quart. Journ. of Med.*, 1910-11, iv, 489.
- <sup>4</sup> HILL AND FLACK. *Journ. of Physiol.*, xxxviii (Proc. physiol. Soc., p. 48).
- <sup>5</sup> HILL AND ROWLAND. *Heart*, 1911-12, iii, 219.
- <sup>6</sup> HILL, FLACK AND HOLTZMANN. *Heart*, 1908-9, i, 73.
- <sup>7</sup> JANEWAY. "The Clinical Study of Blood-Pressure," 1910, 64.
- <sup>8</sup> OLIVER. "Studies in Blood-Pressure," 1904, 2nd edit..















RC  
681  
ALH38  
v.4

Heart; a journal for the  
study of circulation

Biological  
& Medical  
Serials

PLEASE DO NOT REMOVE  
CARDS OR SLIPS FROM THIS POCKET

---

UNIVERSITY OF TORONTO LIBRARY

---

STORAGE



